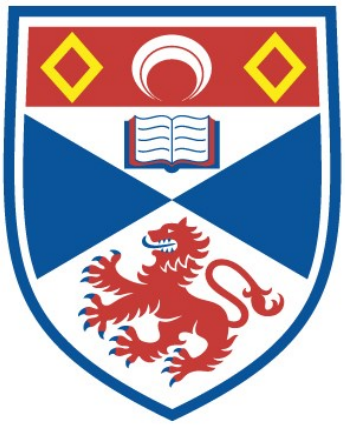
SOME DIHYDRODIAZEPINIUM SALTS AND RELATED COMPOUNDS

Kanwaljit S. Tucker

A Thesis Submitted for the Degree of PhD
at the
University of St Andrews



1978

In the Memory of My Father

SOME DIHYDRODIAZEPINIUM SALTS

AND RELATED COMPOUNDS

being a Thesis

presented by

KANWALJIT S. TUCKER, B.Sc.

to the

UNIVERSITY OF ST. ANDREWS

in application for

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St. Andrews September 1978

Th 9141

DECLARATION

I declare that this thesis is based on the results of experiments carried out by me, that it is my own composition, and has not previously been presented for a higher degree.

The work was carried out in the Department of Chemistry of the University of St. Andrews, under the direction of Dr. D.M.G. Lloyd.

CERTIFICATE

I hereby certify that Mr. Kanwaljit S. Tucker, B.Sc., has spent 11 terms at research work under my supervision, has fulfilled the conditions of the Resolution of the University Court 1967, No. 1, and is qualified to submit the accompanying thesis in application for the degree of Ph.D.

Director of Research

University Career

I entered Queen Elizabeth College, University of London in October 1971 and graduated B.Sc. with Second Class Honours (Division Two) in Chemistry and Physiology in 1974.

The research described in this thesis was carried out between October 1974 and May 1978, during which time I held a Research Studentship awarded by the University of St. Andrews.

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Parts of this thesis could not have been written without the help of Dr. A.R. Butler (Kinetics), Dr. R.K. Mackie (Spectra) and Dr. J. Walton (E.S.R.). I am also indebted to my friends and colleagues in the laboratory particularly Dr. Hamish McNab, for many stimulating and valuable discussions.

My thanks are also due to the technical staff of the department, especially Mrs. M. Smith (n.m.r. spectra), Mr. C. Millar (mass spectra), Mr. J. Bews and Mrs. S. Smith (microanalyses).

I am indebted to Mrs. W. Pogorzelec and Mrs. S. Smith for their help in the production of this thesis.

Finally, I am most grateful to the University of St. Andrews for the award of a Research Studentship.

Summary

A wide variety of 6-aryl-2,3-dihydro-1,4-diazepinium salts has been prepared by reaction of 1,2-diamines with 1,5-diaza-3-aryl-pentadienium salts. The latter compounds were readily accessible by Vilsmeier formylation of the appropriate arylacetic acid. Some dianil salts were also prepared *via* chlorovinyl-aldehydes.

Cyclisation of the 3-aryl substituted vinamidinium compounds is sensitive to the effects of substituents adjacent to the reactive centres. The reaction of the open-chain vinamidinium salts with piperidine suggests that the formation of the 7-membered ring compounds is a two step process, with the rate of cyclisation determined by the second-step. For sterically hindered aryl-vinamidinium salts and/or diamines cyclisation to diazepines was accomplished either by initial treatment of the vinamidinium salt with ammonia followed by addition of the diamine, or by using the sodium salts of arylmalondialdehydes obtained by alkaline hydrolysis of the vinamidinium salts.

Some 6-unsubstituted dihydrodiazepinium salts were also prepared from β-diketones.

The studies of the reactions of 6-aryl-2,3-dihydrodiazepinium salts with electrophiles showed that bromination and nitration occurs at the *p*-position of the 6-phenyl ring, and that the phenyl ring is activated by its diazepine substituent. A substituent adjacent to the bond linking the two rings alters the geometry of the two rings and consequently affects the chemistry of these compounds by diminishing the conjugation between the two rings.

Kinetic studies indicate that substituents at the 2-position and N-positions of the diazepine ring also affect reactions at the p-position of the 6-phenyl ring; the rate of bromination is lowered by the introduction of methyl substituents at the 2-position.

The halogen atom of a 6-(p-halogenophenyl)dihydrodiazepinium salt is not replaced by nucleophiles. 5,7-Unsubstituted-6-aryl-dihydrodiazepines undergo 'transdiazepination' on treatment with substituted ethylenediamine.

The 6-phenyldihydrodiazepinium salt forms a free radical on addition of concentrated sulphuric acid.

The mass spectral fragmentation of these compounds indicates the primary loss of an N_1-C_2 species; other fragmentation patterns are also described.

Some 1,5-benzodiazepines were also studied. They also contain the vinamidinium system, but it is perturbed by a complicated interaction between the two rings. Bromination of these compounds takes place at the 2,4-methyl substituents. Their mass spectra differ from those of the 6-aryldihydrodiazepines; quinoxaline and benzimidazole species are the predominant breakdown products. Some simple macrocycles were prepared from β-diketones and diamines. They also differ from the 2,3-dihydro-diazepines; for example no electrophilic substitution products could be isolated.

The effect of electronic perturbation on the 1,5-diazapenta-dienium system when it is contained in 1,2-dihydro-2-oxo- and 2-thioxo-5-arylpyrimidinium salts was also investigated. They formed adducts with piperidine at their 4-position. Their syntheses

were carried out by reactions of arylmalondialdehydes with dimethyl substituted urea and thiourea. Some of these compounds showed fluorescence.

The electronic structures of 2,3-dihydro-6-aryl-1,4-diazepinium salts, and of the other related salts containing the vinamidinium system which are considered in this thesis, were investigated by ^{13}C n.m.r. spectroscopy.

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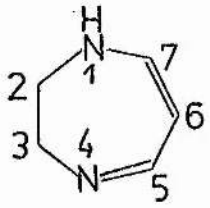
Introduction

The whole range of diazepines has been reviewed by Popp and Noble in 1967[1]. A more detailed survey of the chemistry of 2,3-dihydrodiazepines (1) and their salts and of some related compounds is made here.



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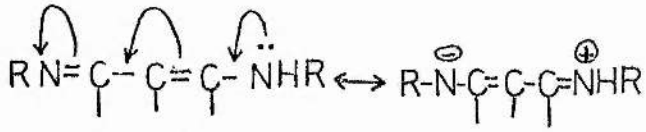


(2)

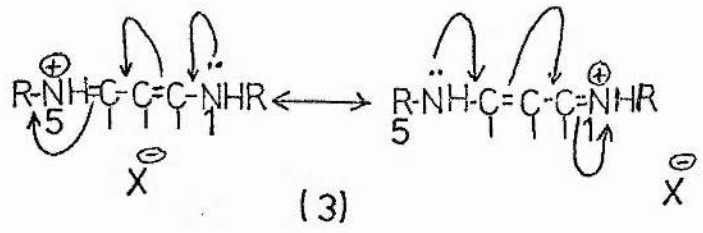
Vinamidines and vinamidinium systems

The 1,5-pentadiene system (2), known as vinamidine[2,3] because it represents a vinylogue of an amidine, is the most important part of the dihydrodiazepine molecule. Thus, this system, together with the derived vinamidinium cation system (3), merits a detailed review.

The vinamidinium system shows some chemical resemblance to benzenoid compounds and displays a quasi-aromatic[4] or meneidic character[5,6]. Meneidic character may be summarised by Robinson's phrase[7], "The tendency to retain the type". Although "Aromatic Reactivity" is one example of meneidic character, the concept may be applied more generally, for instance, carboxylic acid derivatives show retention of type in the interconversion of esters, amides, and halides[6], etc.

In a vinamidine system (2) an amino group acts as an electron-donor group and an imine group acts as the electron-acceptor group. Therefore, this represents a good example of the push-pull alkene system which has received some attention because of the way this system may provide an extra resonance

stability to an otherwise unstable system[8]. The vinamidinium salts (3) are particularly stable because of their symmetry.

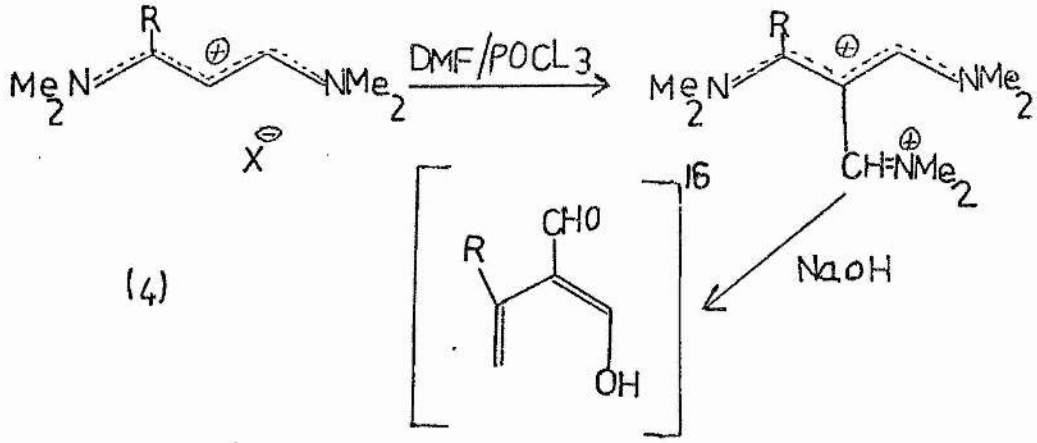


(3)

The two canonical forms are identical and can be compared to Kekulé forms for benzene. The electrons are delocalised within the chains, and this is clearly shown by the vicinal coupling constants in the ^{1}H n.m.r. spectra[9,10]. It has also been confirmed in the case of dihydrodiazepinium salts by X-ray structure determination[11]. ^{13}C n.m.r. studies[12] show that there is an alternation of electron density along the systems; the terminal nitrogen atoms bear the greatest electron density, while the α-carbon atoms are electron poor and the β-carbon atom is electron rich. Calculations which have been made on the vinamidine system are in accord with this data[13,14].

As a consequence of the π-electrons delocalisation in the vinamidinium system, these salts react selectively with electrophiles to give β-substituted products. The α-positions are reactive towards nucleophiles, and this fact has been exploited in the preparation of a wide variety of different compounds (see later). The former represents an electrophilic attack by one cation on another cation[c.f. 15], and this apparent anomaly is easily understood when it is realised that vinamidinium ions are examples of electron-rich cations sharing six electrons over five centres. The following are only a few of the examples

of electrophilic attack at the β-position.



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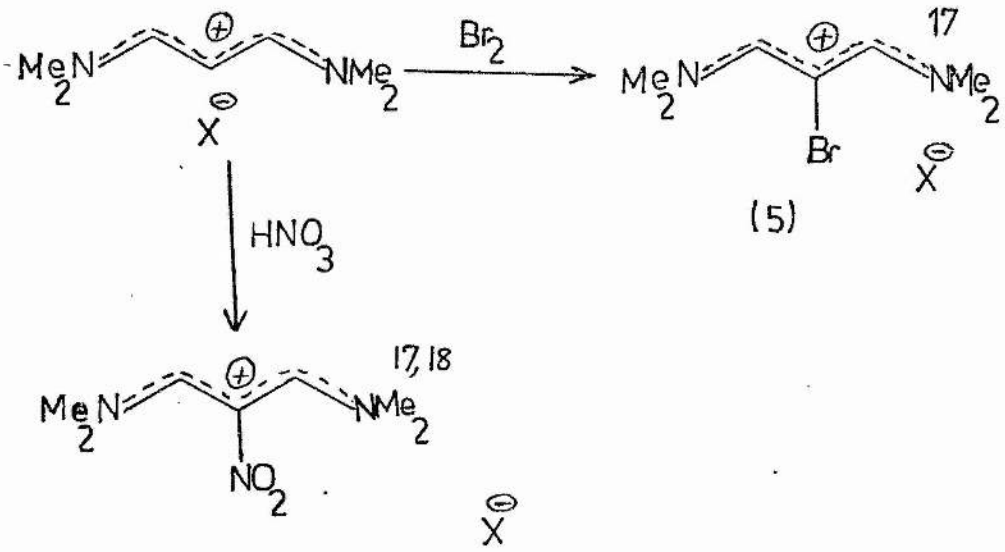

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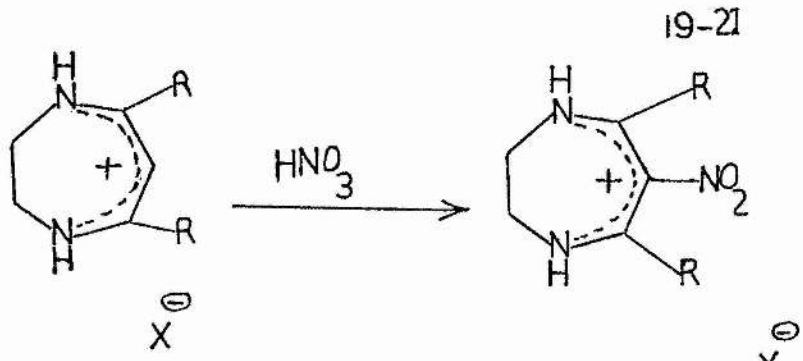
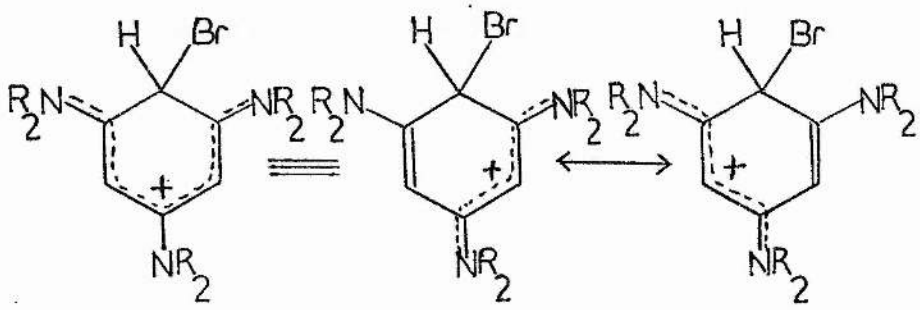


(7)

The electrophilic reactions proceed by substitution involving σ-complexes (Wheland) as intermediates.

The importance of the Wheland intermediate in the course of electrophilic substitution reactions of benzenoid compounds has long been recognised. The benzenium ion itself has been observed spectroscopically in super acid media[22], but the first σ-complex intermediate to be isolated and to be stable at ambient temperatures, i.e. (8)[23], used a vinamidinium system, and thus the concept of push-pull mesomeric stability, to provide the necessary stabilisation energy.



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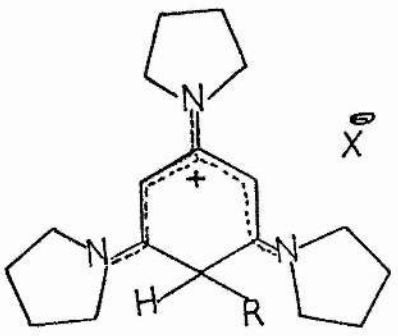
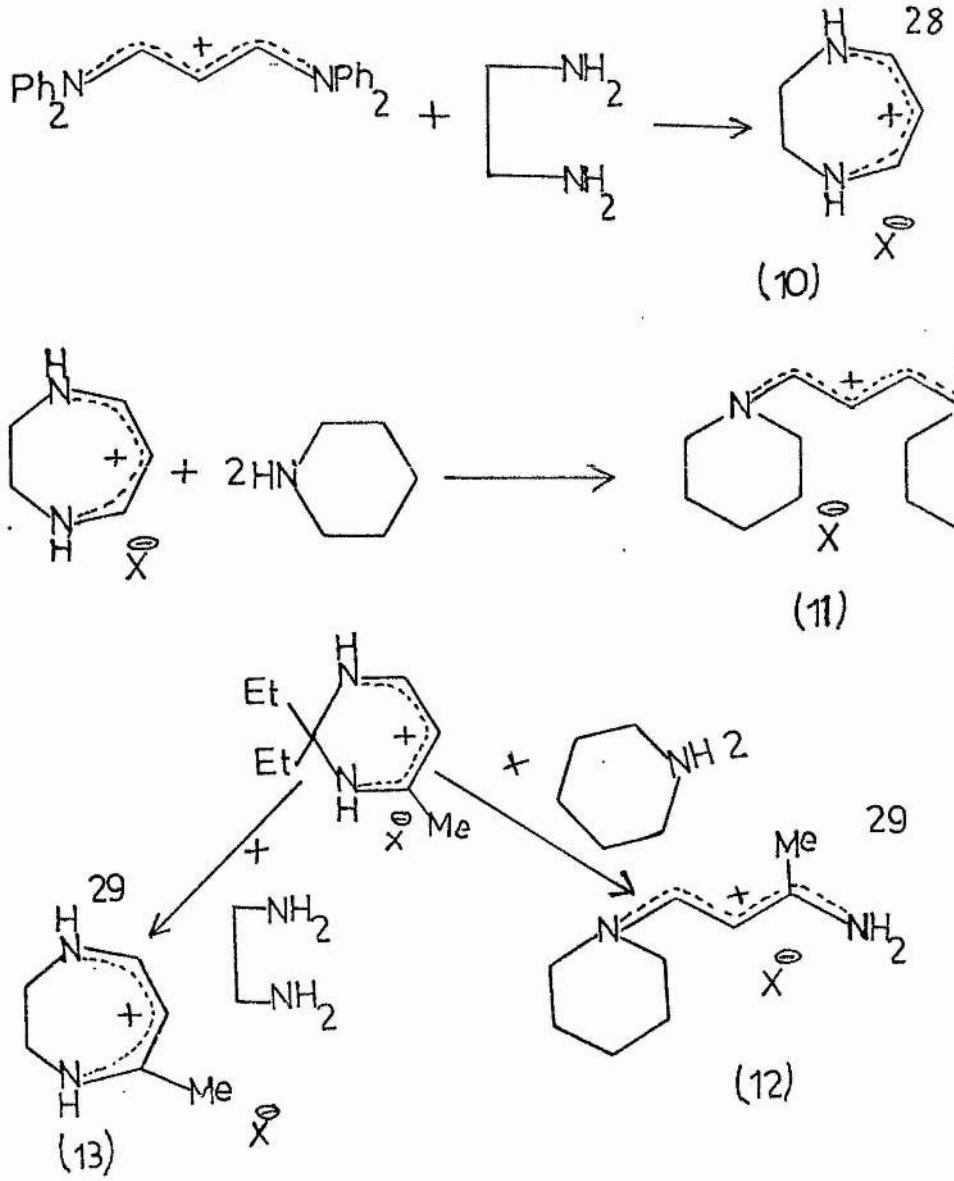


(R=ACETYL, BENZOYL, p-$CH_3C_6H_4SO_2$)

(9)

It is interesting to note that halogeno-benzenes are produced by the action of bases on the cation (8), whereas strong nucleophiles cause debromination[24] in a manner reminiscent of dihydrodiazepines[25] and tetrahydrocorrins[26]. Deprotonation of the Wheland intermediate[27] (9), recently isolated, is effected with N,N-diisopropylethylamine, but the cleavage of the R-group is observed with sodium methoxide.

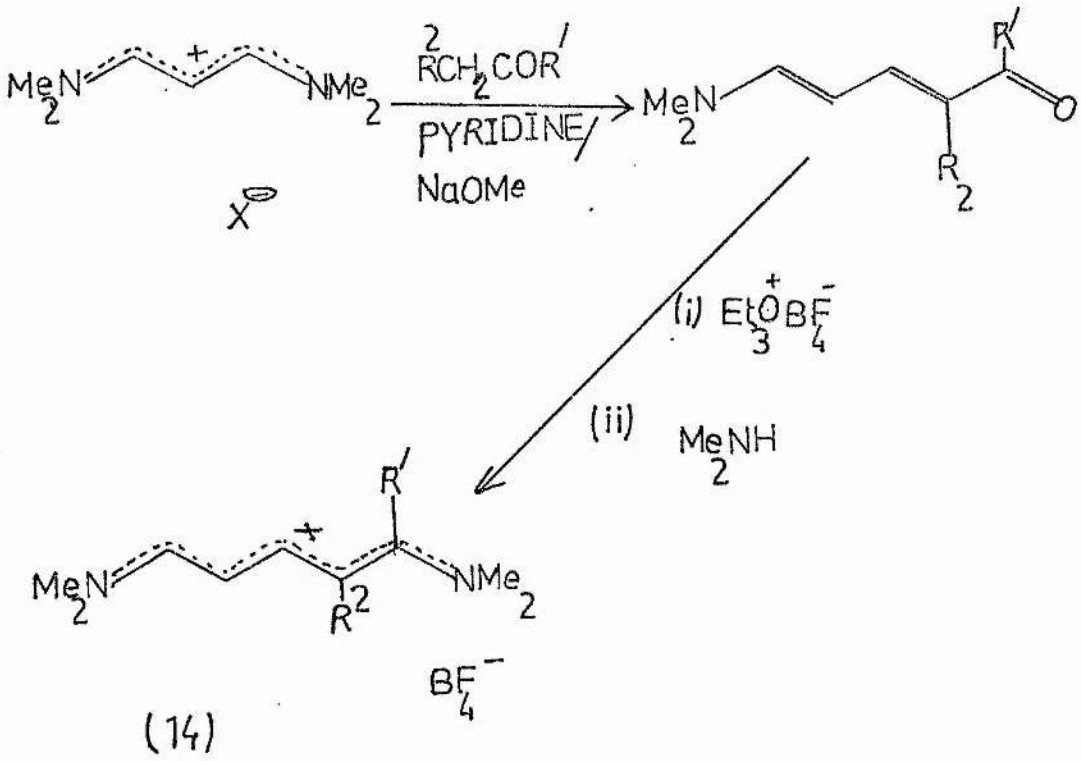
Reactions of vinamidinium salts with nucleophiles have been carried out in order to prepare other types of compounds as depicted below (10-13).



A great deal of literature is available on these open chain diazapentadienes and their higher vinylogues. They will react with thiols to give methine dyes[30], with heterocyclic immonium salts with acidic C-H to give pentamethine[31-39] dyes, which have assumed importance as sensitisers of photographic silver halide emulsions[40] and as models for investigating the influence of substituents on the u.v. and visible spectra of polymethine[37,38,41] dyes. There is an enormous literature available in this field, a review on cyanines comments that they "have made colour photography and high speed photography possible"[40]. They have also been used as synthetic intermediates, e.g., in the preparation of phenanthrenes[42], quinolines[43], cyanines[31], pyrazoles[44-45], dihydrodiazepines[28,46], and pyrimidines[47]. The preparation of the parent salt (10) is presently[28] only accomplished in satisfactory yield by such a method.

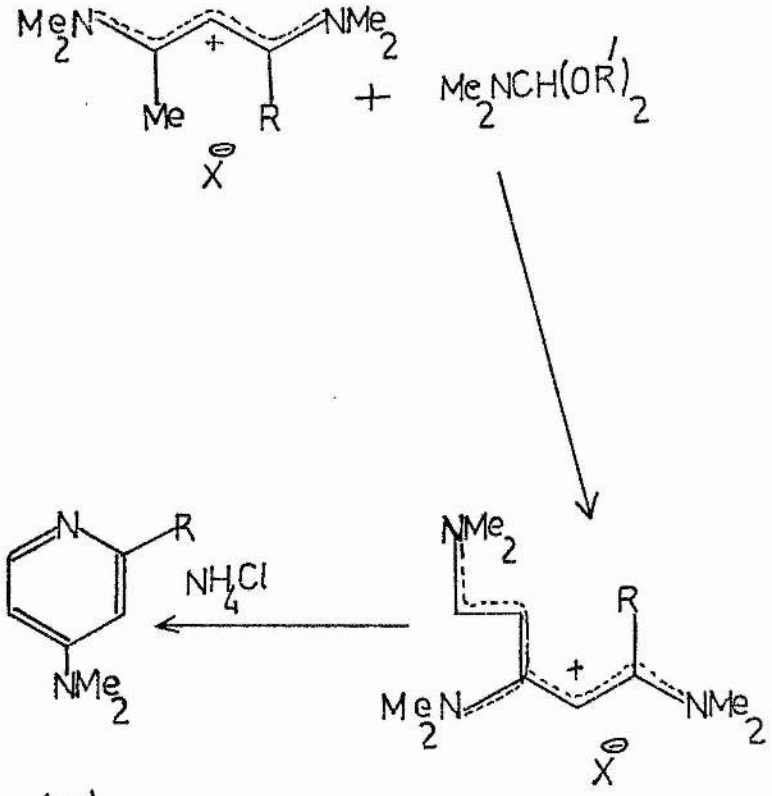
Carbon nucleophiles react with vinamidinium salts in an analogous fashion to nitrogen nucleophiles. The carbanions derived from α-methyleneketones displace one of the amino groups of vinamidinium salts to give δ-amino-pentadienones[48] which can be further converted into vinylogues of vinamidinium salts.

α-Methyl groups of vinamidinium salts have potential carbanionic reactivity like that of α- and γ-methyl groups in pyridinium ions; but the synthetic usefulness has not been explored yet.



(14)

The following example has been reported[49].

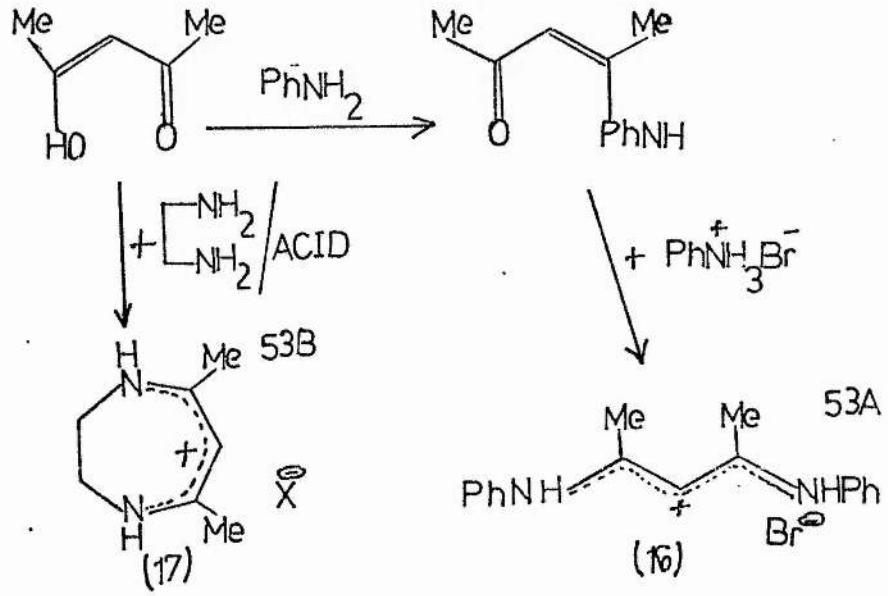


(15)

The use of the 2,4-dichloro derivatives of vinamidinium salts in the synthesis of a variety of heterocycles has recently been reviewed[44].

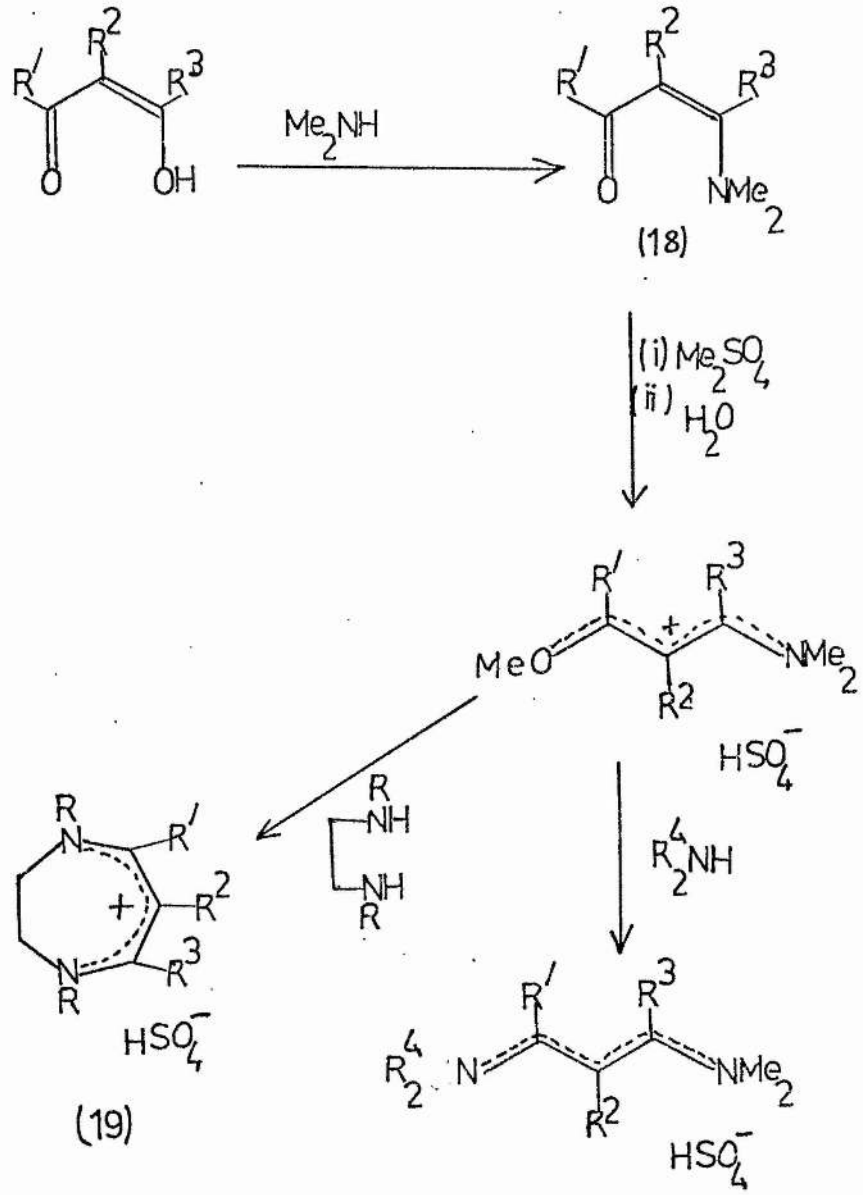
Preparations of vinamidines and vinamidinium salts

A variety of methods of preparation of vinamidines and their salts has been recorded. In certain cases, they may be made directly from the corresponding dicarbonyl compound or its mono[50,51] or diacetal derivatives[52,53], but two steps may be necessary.

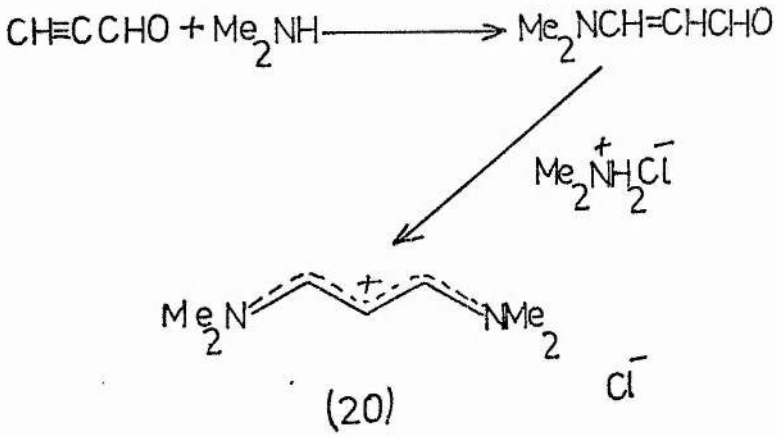


A slightly modified method involves the following scheme[54]: the diamine provides the cyclic vinamidinium salt (19).

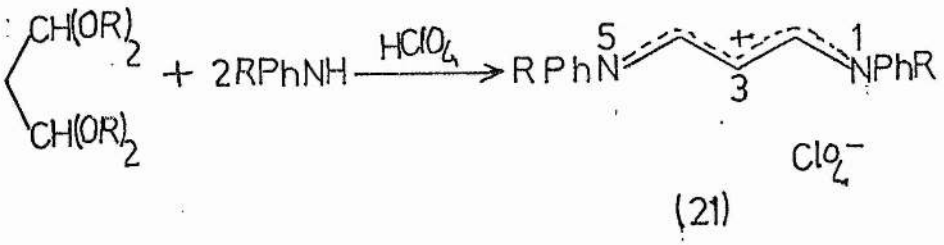
A common route to N,N'-dialkyl-2,3,4-unsubstituted vinamidinium salts involves successive Michael addition, and



condensation of an alkylamine with propargylaldehyde[55].

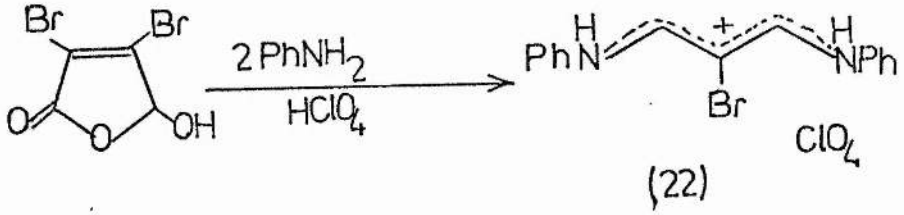


The unsubstituted N,N'-arylvinamidinium salts, e.g. (21) have been prepared from the tetraacetal of malondialdehyde[28,52].



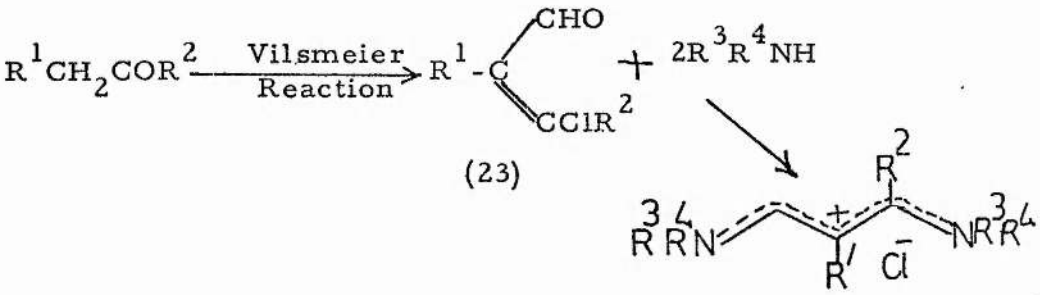
(21)

β-Halovinamidinium salts (22) have been prepared from mucobromic and mucochloric acids, which are masked β-dicarbonyl compounds[56,57].



(22)

β-Chlorovinylaldehydes (23), which may be considered as the acid chlorides of the enol forms of β-dicarbonyl compounds, have also been used as the starting materials for the preparation of vinamidinium salts[43,58-62].

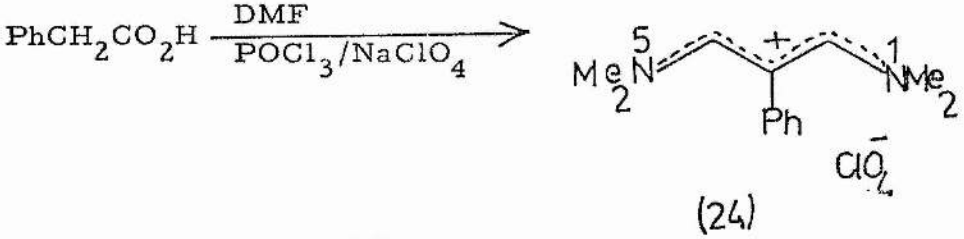


(23)

Vinamidines have also been prepared from β-chlorovinylketones[63-68].

A good general method for the preparation of the β-substituted vinamidinium salts utilises the Vilsmeier formylation of aldehyde acetals[69], haloacetic acids[18,70-74], cyanoacetic acids[17], malonic acids[75] or phenylacetic acids[18,73,74]. The mechanism of formylation from the acids is not fully understood but must

involve diformylation coupled with decarboxylation, e.g. (24).

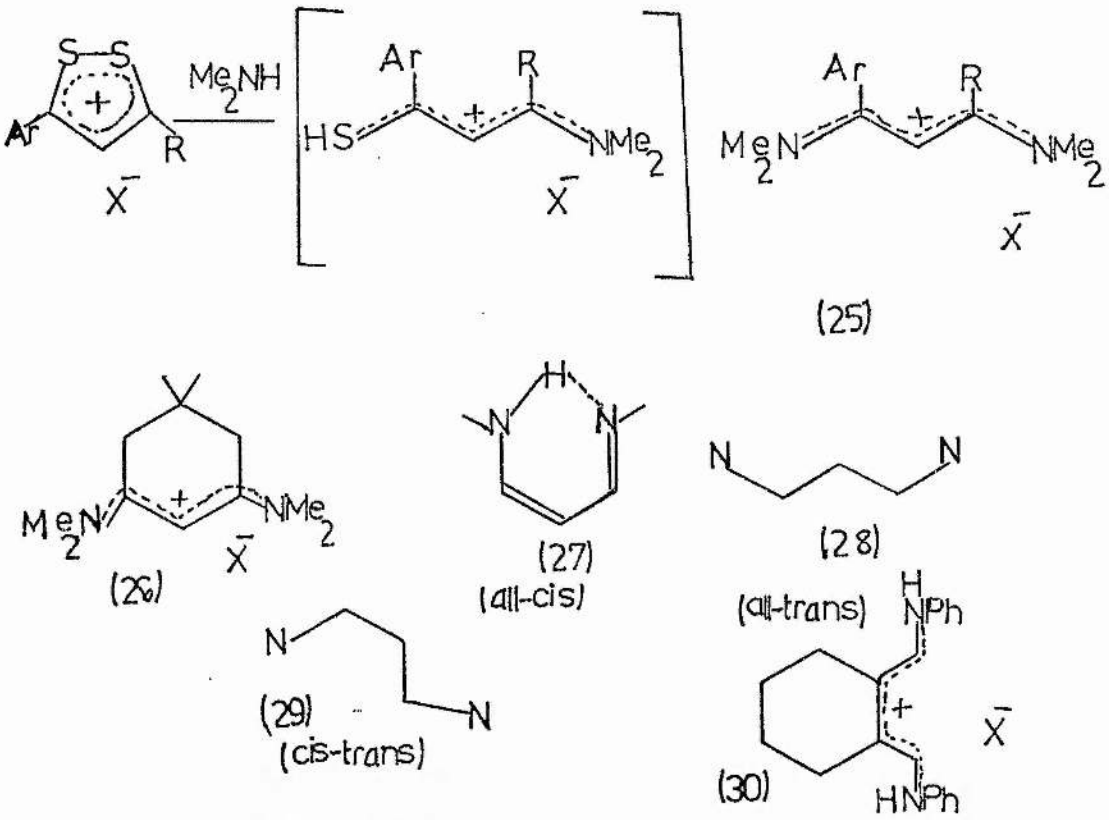


(24)

α-Cyclohexenyl[76], β-alkoxy[77], and β-aminovinamidinium[77] salts have also been prepared by Vilsmeier formylation. α-Amino- and α,α'-diaminovinamidinium salts have been obtained by addition of an α,α-diaminoethylene to a formamidinium salt, and to an unsubstituted vinamidinium salt, respectively[78]. However, no attempts have been made to obtain the cyclised vinamidinium salts from these compounds.

2,4-Dichlorovinamidinium salts have been obtained from phosgeneimmonium[45,79-80] salts. Cyclisation of this dichloro-compound was attempted (see later, discussion). Monochlorovinamidinium salts have been prepared by addition of phosgene-immonium salts to enamines[44], and by means of a Vilsmeier reaction from N,N-dimethylamides containing two α-hydrogen atoms[73-74]. Dibromovinamidinium salts are obtained by the action of hydrogen bromide on malononitrile[81].

The preparation of 2-aryl and 2,4-diaryl-1,5-diaza-pentadienes from dithiolium salts[82] (25), and the isolation of the 3-methyl-1,5-diphenyl compound via a six-stage synthesis from iso-butraldehyde[83] are two examples of non-general methods.



Conformation of vinamidinium salts

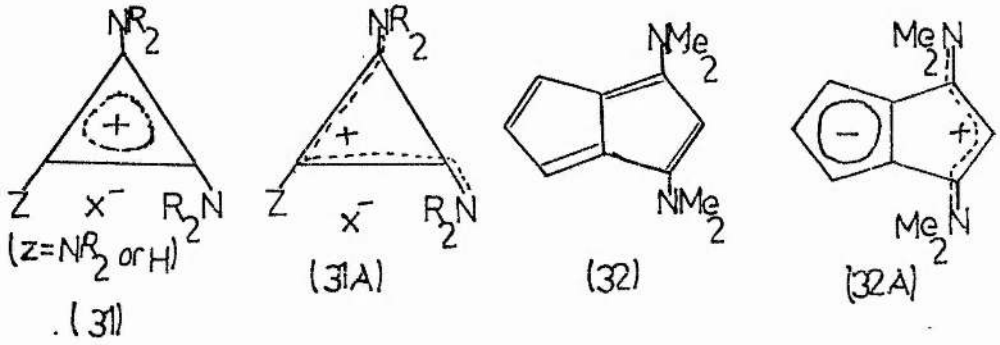
Vinamidines and vinamidinium salts may be open-chain (3) or included in a ring system (26) and in the dihydrodiazepinium salts (7). Thus, depending on their environment the vinamidine system can adapt one of the three distinctive geometrical shapes. Open-chain vinamidines having a NH-group exist predominantly in the all-cis('U')-shape[52, 84-86] wherein they are stabilised by intramolecular hydrogen bonding (27), as are β-diketone enols. The possibility that these bases possessed a non-classical cyclic delocalised system of 6 π-electrons involving the N-H bonds[50] has been ruled out[87], they are indeed hydrogen-bonded vinamidines. On the other hand, their salts take up all trans ('W')-configuration, e.g. (21). This is shown quite unambiguously by the large vicinal coupling constants

(J ca 1.3 Hz) of protons 1-5 in the n.m.r. spectra[86, 88-89].

Cyclic vinamidines have their configuration forced upon them by the shapes of the rings in which they are incorporated. Hence, dihydrodiazepines (7) must have a U-form, while the dianil derivatives[18, 43, 86] (30) are probably cis-trans ('sickle')-shaped. Vinamidines of the latter type have been prepared photochemically from those of the 'W'-structure[46, 86] but very little work has been published.

Some special vinamidinium and related systems

Di- or triaminocyclopropenium salts (31) and diamino-pentalene (32) may also be stabilised by the contribution of vinamidinium systems.

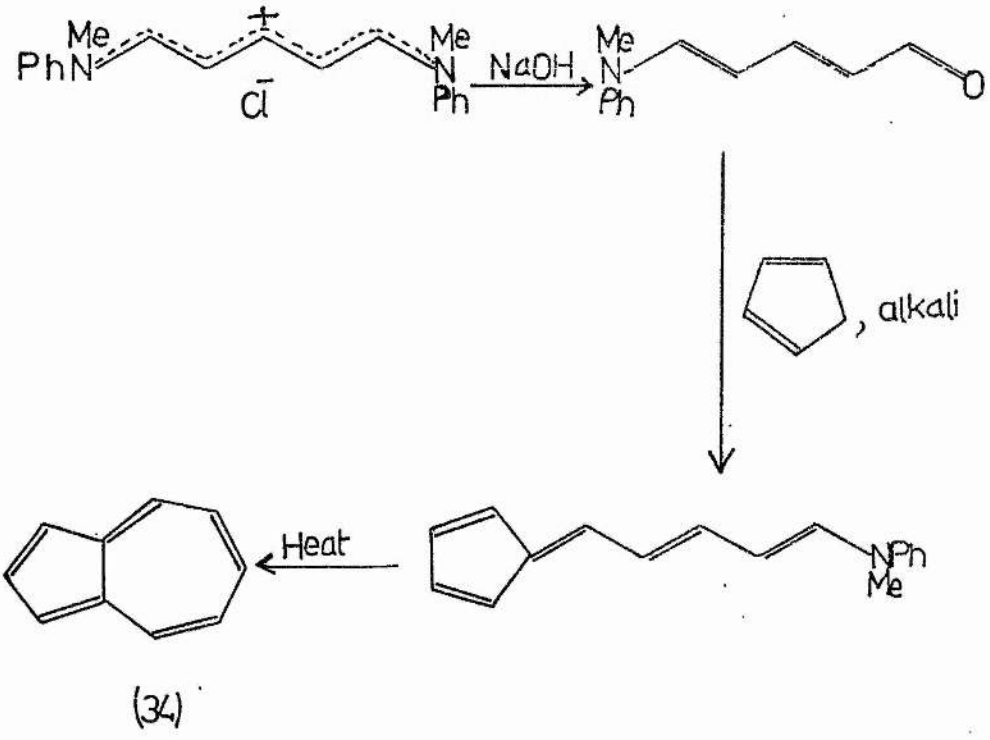


1,3-Bis-(dimethylamino)-pentalene (32) is stable in air for some hours as opposed to simple pentalene derivatives which have recently been prepared[90]. It is thought that the contributing factor is the vinamidinium cyclopentadienide canonical form[91] (32A). Cyclopropenium salts react additively in the cold with weak nucleophiles[92, 93] (e.g. alcohols) but the derivative [(31), $Z=NR_2$] is stable in air and in particular is resistant to attack by hot water[94,95]. This stabilisation might be due to the contribution of the bridged-imine canonical form (31A)[96]. It has recently[97] been shown that

the 1,2-diaminocyclopropenium system undergoes an electrophilic attack at the 2-position of the ring, which is electron rich, in keeping with its pronounced vinamidinium character. The corresponding trialkoxy[98] and tris(alkyl-thio)cyclopropenium[99] salts are markedly less stable.

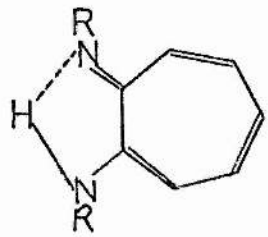
The polymethinium salts (33) are vinylogues of vinamidinium salts and like them adopt the ('W')-configuration[88]. The glutacondialdehyde derivatives (33, n=5) are readily prepared in two steps by the action of amines on pyridinium salts[55]. The reverse process has also been reported[100]. Glutacondialdehyde dianils are important synthetic intermediates, and are used in the classic Ziegler-Hafner synthesis of azulenes[101-103] (34).

(33)



(34)

All-trans diazanonamethine has not been studied chemically but the isoelectronic cycloheptatriene derivatives (35) have been investigated. These are readily obtainable by the action of the appropriate amine on the 1,2-diethoxytropylium[104] ion. Other methods of preparation are also available[105-107].



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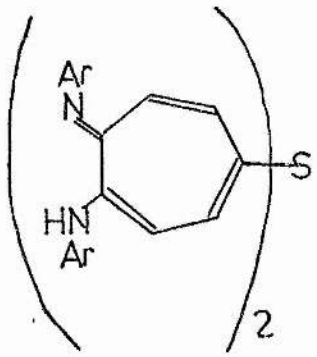
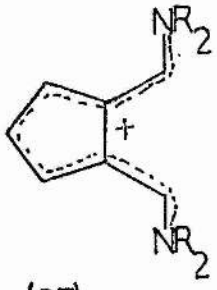


(36)

These bases show meneidic character; they may be halogenated and coupled with diazonium salts at the 4-position[105]. 4-Halogeno substituents are displaced by nucleophiles, for instance, with either hydrogen sulphide or thiourea the sulphide[105] (36) is obtained. No reactions have been carried out on their salts.

The cyclopentadiene derivatives (37)[108] and (38)[109] are also examples of 1,7-diazacyclononatetraenes. A detailed analysis of the spectra of the base (38) was interpreted in terms of an intramolecular hydrogen bond, which undergoes rapid exchange[110]. These conclusions have been confirmed recently by an x-ray crystal structure determination on compound [(38), R=Ph][111].



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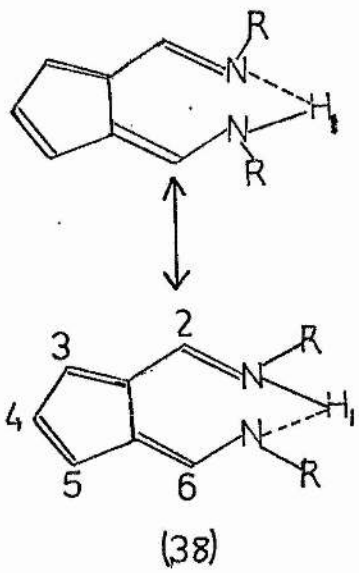

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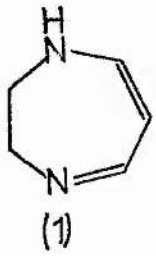
2,3-Dihydro-1,4-diazepines and 2,3-dihydro-1,4-diazepinum salts



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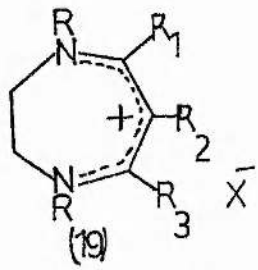

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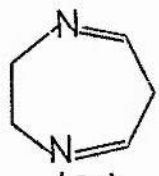
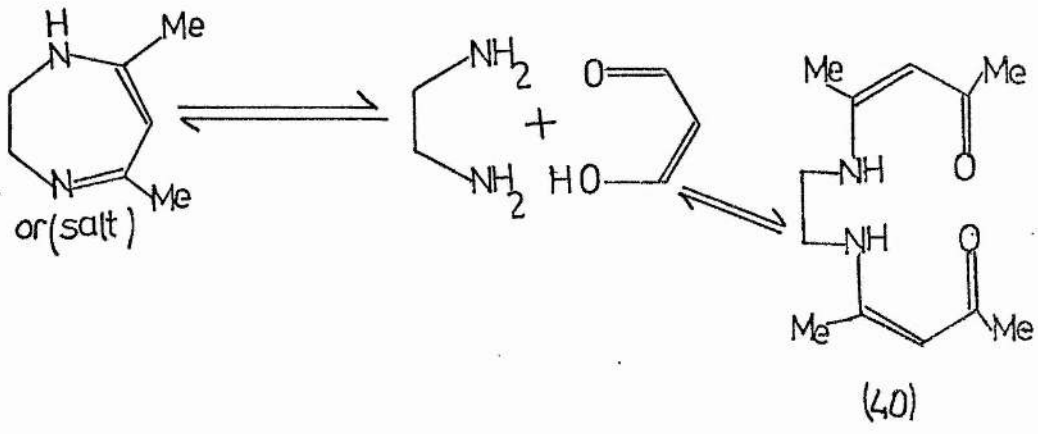


(39)

2,3-Dihydrodiazepines (1) and their salts (19) remain today perhaps the most extensively studied vinamidine system. 2,3-Dihydrodiazepines have recently been reviewed[112] comprehensively, thus, only the salient features of their chemistry are mentioned here. Spectroscopic data show that dihydrodiazepines normally exist in the conjugated form (1) rather than the tautomeric bisimino form (39).

Preparation of dihydrodiazepines

Schwarzenbach and Lutz[53B] (1940) obtained the first dihydrodiazepine by condensation of acetylacetone with ethylenediamine. The reaction between β-dicarbonyl compounds and 1,2-diamines has remained the common method for the preparation of these compounds, although modified conditions may be essential[51,53], especially in the preparation of aryl substituted compounds[113-115]. The differences may be due to the lower reactivities of aryl substituted carbonyl groups[113]. When condensation of acetylacetone with C,C'-tetramethylethylenediamine was attempted, the only product isolated, in high yield, was the acetylacetone salt of the diamine[116] (see discussion later). The course of the reaction is pH dependent. Indeed, some earlier workers[117] had described the formation of only the bisoxoenamine (40) from these reactants, while other workers[118] had reported the preparation of the diazepine but quoted physical constants which are those of the bisoxoenamine. The structure of these alternative open-chain products, e.g. (40) as bisoxoenamines rather than as tautomeric diimines, was later confirmed by n.m.r. spectroscopy[116,119].



(40)

The bisoxoenamine (40) is obtained at room temperature as the major product in neutral or mildly alkaline conditions but at higher temperatures its yield drops sharply even at the most favoured pH values[120] for its formation.

Examples of the preparation of dihydrodiazepines by other methods have appeared in the literature, e.g., the acid salt of the bis(N-methylanil) of malondialdehyde reacts with N, N'-dimethylethylenediamine to give a dihydrodiazepinium salt[46], while the unsubstituted dihydrodiazepinium cation is best prepared by the reaction of the dianil, or preferably, the bis(N-phenylanil) of malondialdehyde with ethylenediamine[28].

Dihydrodiazepines have also been prepared by methods not involving the use of condensation reactions. Thus, 5-methyl-dihydrodiazepine has been prepared by addition of ethylenediamine to buta-1, 3-diyne[121] and 1-methyl-2-oxodihydrodiazepines have been obtained by dehydrogenation of 2, 3, 6, 7-tetrahydrodiazepines with benzoyl peroxide and N-bromosuccinimide[122]. 2, 3-Dihydro-diazepines have been prepared by heating the bisanils of 1, 2-diaminocyclopropanes[123-125], a reaction involving a Cope rearrangement.

Stability and general properties of dihydrodiazepines

Dihydrodiazepine bases, with amidines, are perhaps the strongest organic bases known, with pKa values in the region of 13-14[53B]. This may be ascribed to the formation of a symmetric delocalised system of π-electrons in the derived cation, whose resonance energy is estimated to be ca 20 Kcal mol^{-1} [126]. The stability of the cations is further exemplified by the large pH

range over which the monocation form is the predominant species. The dication is formed significantly only in acids of strength comparable to 70% sulphuric acid[119]. Calculations based on pK data suggest that dihydrodiazepine bases have 8 Kcal mol^{-1} less energy than the corresponding cations. (This is in accord with the asymmetry of the conjugated system in the bases). This, however, still leaves a resonance energy of ca 10-12 Kcal mol^{-1} compared with the non-conjugated bisimine structure (39).

Dihydrodiazepinium salts are generally resistant to oxidation, dehydrogenation, and hydrolysis[119], although the latter may occur under strongly alkaline conditions. Sodium hydroxide and benzoyl chloride bring about a cleavage to form dibenzoylethylenediamine[119]. With 6-methyl or 6-bromo-substituted salts hydrolysis takes place more easily in acid conditions[127-129]. 6-Nitro- and 6-amino-dihydrodiazepines are not isolable, for their salts are hydrolysed in the presence of alkali[21]. The isolated product (41) is an example of the product of hydrolysis of a 5,7-dimethyl-1,4-phenyldiazepinium salt[115] with aqueous sodium hydroxide.

$$MeCOCH{=}CMe\text{-}NPhCH_2CH_2NHPh$$

(41)

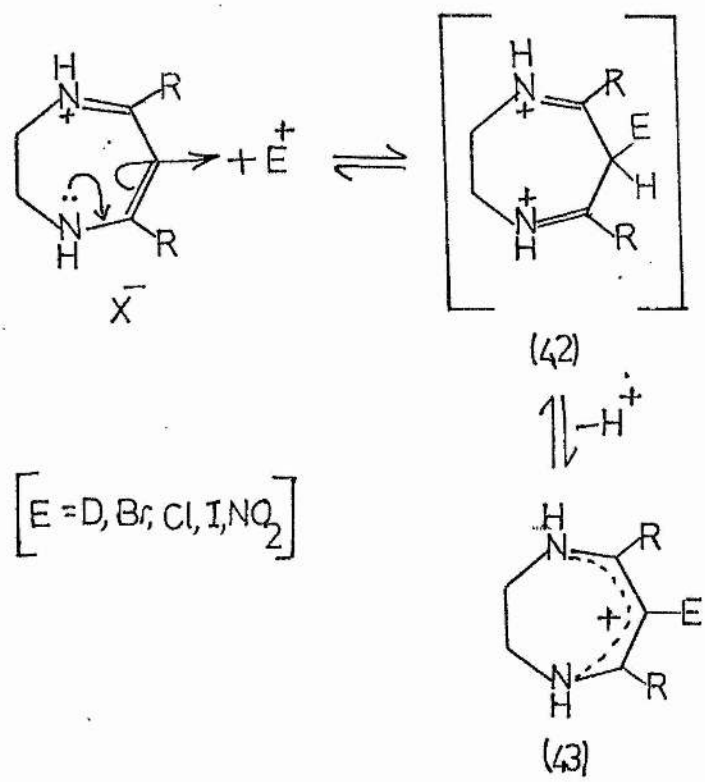
One example of a catalytic reduction of a dihydrodiazepine has been reported[121]. The action of excess sodium tetrahydroborate on polymethinium salts has also been reported, and it proceeds by reduction of the double bonds of the iminium and enamine groups[130]. The detailed chemistry of the dihydrodiazepine

bases, however, still remains to be investigated.

Electrophilic substitution reactions of dihydrodiazepinium cations

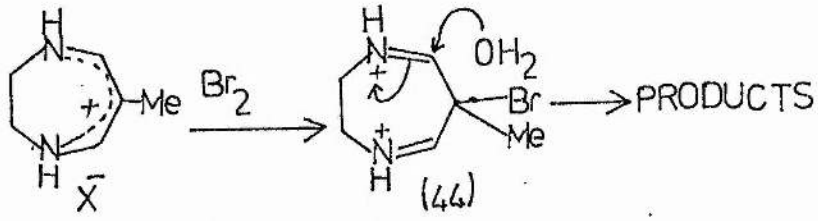
The properties of dihydrodiazepinium cations can be understood in terms of the vinamidinium system which forms an essential part of the molecule. Unless the sp^3-carbon skeleton of dihydrodiazepinium cations produces any modifications of the vinamidinium system, these cations are likely to show properties of a vinamidinium cation. Dihydrodiazepinium cations are electron-rich and are reactive towards electrophiles despite their positive charge. Thus, they can be readily deuteriated by deuterio acids[125,127,131,132], brominated[25,128] with bromine in methanol, halogenated with N-halogenosuccinimides in chloroform or acetic acid[25], and nitrated by nitric acid-sulphuric acid mixtures[21,133-135]. They are also reactive enough to couple with diazonium salts even though the diazodihydrodiazepines so formed are hydrolytically unstable and were not isolated[136]. These reactions characteristically occur at the 6-position and proceed via an intermediate σ-complex (42), analogous to the Wheland intermediate in the electrophilic substitution of benzenoid compounds[112]. This intermediate dication loses a proton to give the 6-substituted product (43).

Kinetic studies[129,131,137] indicate that these reactions closely resemble those of activated benzenoid compounds such as phenols and amines. Hence, the term 'quasi-aromatic' was defined to describe them[4]. Kinetic studies have also shown that the dihydrodiazepinium cation is indeed involved in these electrophilic substitution reactions, so that the nitration reaction



represents a rare example of electrophilic attack by a cation on another cation. Further similarities with benzenoid compounds are also observed, e.g., 6-nitro compounds may be reduced to amines[21,138], which yield stable anils and diazonium salts[21].

Similar stable intermediate dication structures cannot be drawn for electrophilic attack at the 5- and 7-positions and kinetic studies of the bromination of dihydrodiazepinium salts indicate a ratio of reactivities, of at least $1:10^{9}$ at the 5- and 7-positions to the 6-position respectively[127,129]. Even 6-methyl dihydrodiazepinium salt reacts preferentially at the 6-position rather than at the 5- and 7-positions[129]. The resultant products are hydrolysis products since the dication intermediate (44) has no mesomeric stabilisation and cannot gain such stabilisation by loss of proton, and, as a bisiminium salt, is readily hydrolysed.



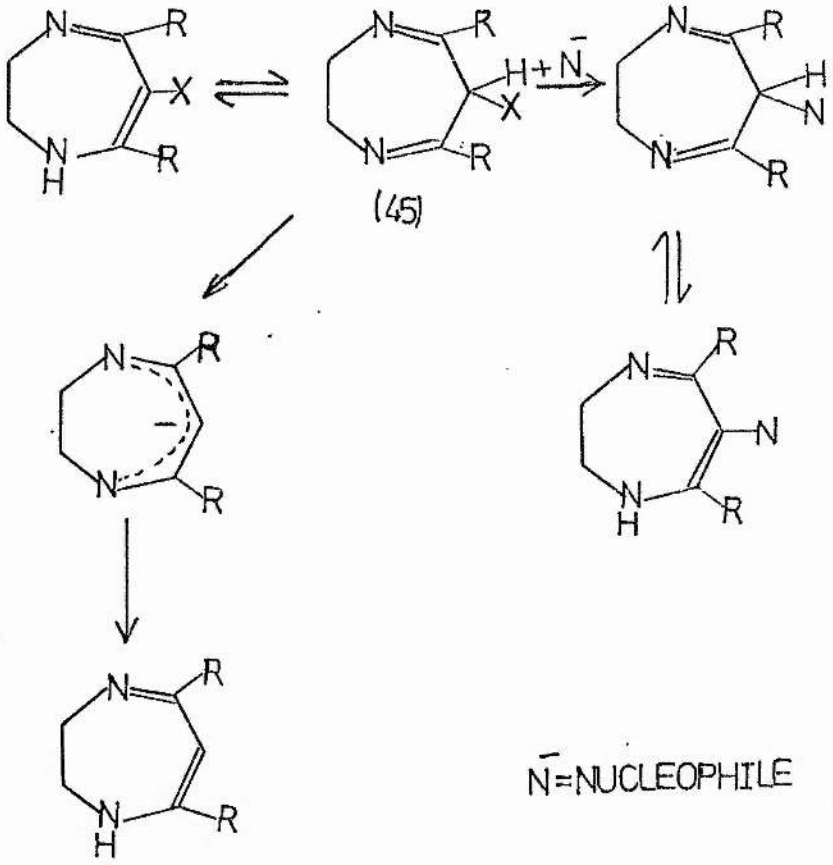
(44)

Nucleophilic reactions of dihydrodiazepinium salts

5,7-Disubstituted dihydrodiazepines are inert to nucleophiles at the 5(7)-positions even though attack at these sites is electronically favourable. However, 5,7-unsubstituted dihydrodiazepines may be attacked by nucleophiles, e.g., N,N'-dimethylethylenediamine (in excess) reacts with the totally unsubstituted dihydrodiazepinium salt to give an N,N'-disubstituted derivative.

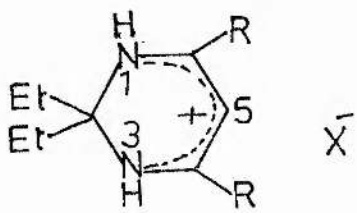
6-Halogenodihydrodiazepines react, unexpectedly, by substitution, with a variety of nucleophiles[25,128,140] such as methoxide and thiourea to give 6-substituted products. Since the conjugated tautomer of the dihydrodiazepine is electron-rich at the 6-position, it is suggested that the bis-imine tautomer (45) may be involved. In the bisimine tautomer the 6-position is adjacent to three electron withdrawing groups and is thus susceptible to nucleophilic attack (Scheme 1).

N-Substituted-6-halogenodihydrodiazepines cannot exist as a bis-imine tautomer and they do not react with nucleophiles[25] in this way. There is, however, no spectroscopic evidence for the presence of any bis-imine tautomer, although energetic considerations suggest that it might be present to the extent of ca. 10%. The concentrations may be too small to be observed spectroscopically because of rapid exchange.



(Scheme 1)

Protodenalogenation is an alternative competitive reaction with the conventional nucleophilic substitution at the 6-position and occurs particularly when the site of reaction is sterically crowded due to large X, R, or N^- (see Scheme 1)[25, 139]. Attack of the nucleophile on the 6-halogen atom in the bis-imine tautomeric form is thought to yield an anion which abstracts a proton from the medium to give the isolated product.



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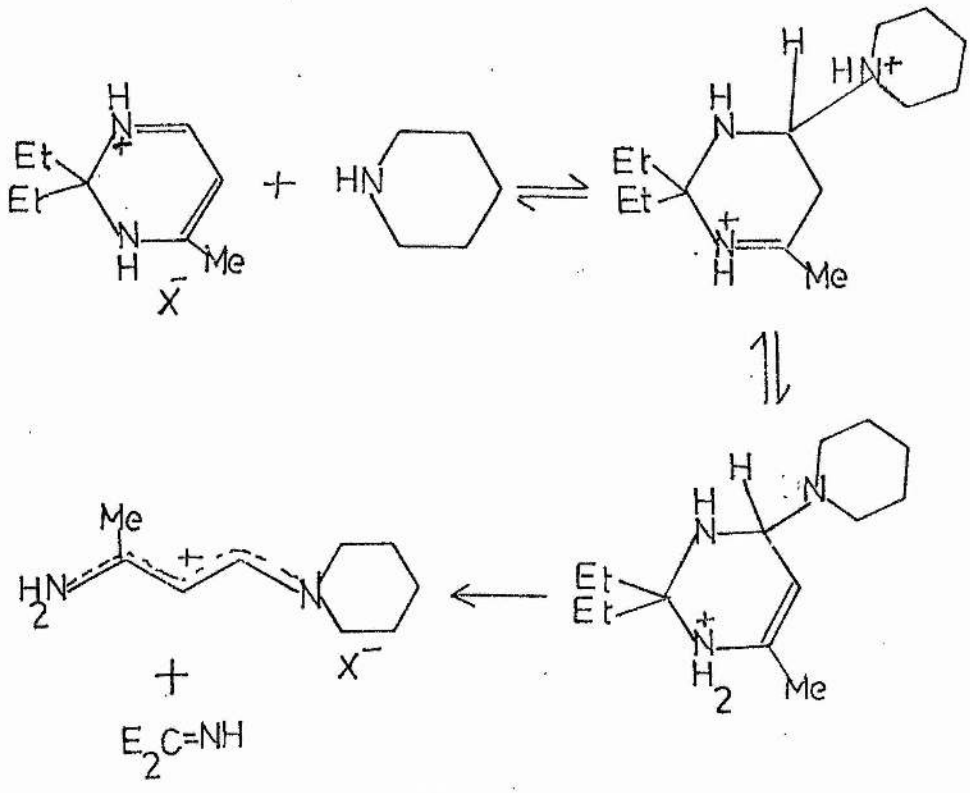
Properties of some other cyclic vinamidinium compounds related to dihydrodiazepines

This thesis is largely concerned with the effect of the geometric and electronic environment on the properties of vinamidines and particularly of 6-aryl substituted dihydrodiazepines. It is therefore appropriate at this stage to consider a selection of other recent examples where these properties are evident.

1,2-Dihydropyrimidines which have recently been reviewed[29] provide one such example. They have been made by the reduction of a pyrimid-2-one[140], and by a condensation reaction involving a ketone, an oxo-acetal, and ammonia in the presence of ammonium nitrate[141]. The mechanisms for this latter reactions are not understood. Dihydropyrimidinium salts (46) display a number of similarities with the dihydrodiazepinium ions. For example, they undergo electrophilic substitution at the 5-position which is an equivalent of the 6-position of the dihydrodiazepinium ions. Thus they are deuteriated in deuterio trifluoroacetic acid and are brominated by elemental bromine in methanol. N-Halogeno-succinimides also react at the 5-position to give 5-chloro, bromo, and iodo-derivatives.

These halogenated compounds show a bathochromic shift of 20-25 nm in the electronic spectrum, which is also observed for dihydrodiazepinium salts[25,51,128]. There is tentative evidence that these dihydropyrimidinium cations couple with p-nitrobenzenediazonium tetrafluoroborate[29]. 5-Bromo-4-methyldihydropyridinium salts can be debrominated with thiourea[29]. However, the 5-chloro-4,6-dimethyl analogue remains unchanged[29].



(Scheme 2)

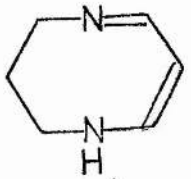
The latter is in direct contrast with the behaviour observed with the 6-chloro-5,7-dimethyldihydrodiazepinium salts[139] where nucleophilic substitution takes place. This may be due to the absence of vicinal crowding in the 6-membered ring compound which has smaller internal bond angles. Lack of vicinal crowding of the 6-halogeno-substituent in dihydrodiazepines has been shown to remove the reactivity of the substituent towards nucleophiles[10].

The 5-methyldihydrodiazepinium ion remains unchanged with N-nucleophiles but the 4-methyldihydropyrimidinium salt reacts with N-nucleophiles to displace part of the molecule and form an open-chain diazapolymethinium system as shown in Scheme 2[29]. 1,2-Dihydropyrimidinium salts, unlike dihydrodiazepinium derivatives, undergo methylation with methyl iodide

to give di-N-substituted products[29].

The dihydropyrimidinium ions are readily protonated and with trifluoroacetic acid they form an equilibrium between the monocation and the dication[29]. The monocations form dications with weaker acids than do dihydrodiazepinium cations and thus must be stronger bases than the dihydrodiazepinium ions. No measurements of their pKa values, however, have been made, and also no dihydropyrimidine base has been isolated.

Because of the different angles in the dihydropyrimidinium salts, the vicinal coupling constants are smaller ($J_{1,6}$ 6.8; $J_{5,6}$ ca 6) than in the 7-membered ring compounds ($J_{1,7}$ 7.8; $J_{6,7}$ ca 8.25).



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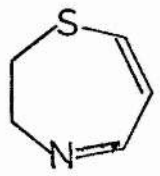


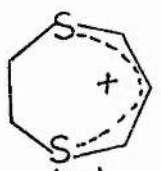
(48)

2-Oxo- and 2-thioxo-1,2-dihydropyrimidinium salts are also known[47]. These compounds, in general, show a diminished reactivity towards electrophiles, presumably due to competitive sharing of the excess electrons of the vinamidinium system by the $\overset{X}{\overset{\|}{NC}}$-N (where X=O,S) moiety (see later, chapter on these types of compounds).

It is apparent from the foregoing account that the properties of the vinamidinium systems incorporated in these cyclic compounds may be affected by their geometry and their electronic environment. When a comparison is made with the eight-membered ring analogue,

1,2,3,4-tetrahydrodiazocine (47), it would appear that the sp^3-hybridised groups linking the ends of the conjugated chain may distort it sterically, and molecular models indicate that the structure is strained. An attempt was made to synthesise an eight-membered ring compound, but such a system still remains unprepared.

Other hetero-analogues of dihydrodiazepinium and dihydropyrimidinium salts are known. For example, the 2,3-dihydro-1,4-thiazepine ring (48) has generated a great deal of interest because of its similarity to penicillin derivatives, and three very specialised derivatives have been reported in the literature[142-144] including a thiazepinium salt[144]. These derivatives are all substituted in the 6-position and their reactions have not been studied. So far, 2,3-dihydro-1,4-dithiepinium cation (49) and dihydro-oxazepine systems (50) remain unknown. The only 1,4-dioxepin derivatives which have been prepared contain the 5,6,7-trihydrodioxepin nucleus (51)[145]. No simple derivatives



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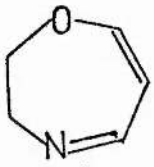

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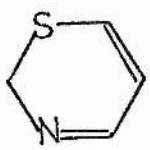
(51)

of (52), 2H-1,3-thiazine, have been isolated, but 2-ethoxy-2H-1,3-oxazine (53) has been prepared by the reaction of oxoenamines with triethylorthoformate[146]. Its reactions remain to be studied. It is tempting to postulate that these compounds containing heteroatoms with diminished electron-releasing power may well behave quite differently to the dihydrodiazepines and the



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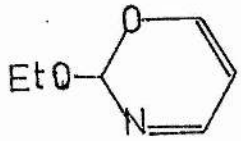
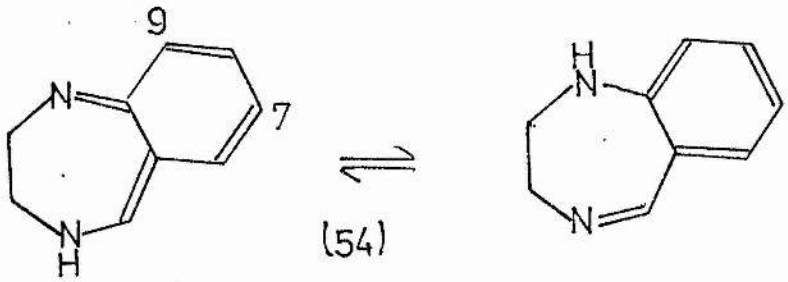


(53)

dihydropyrimidines.

2,3-Dihydrobenzo-1,4-diazepines (54) have been studied extensively[147] because of the pharmacological importance of certain derivatives such as 'Valium' (55)[148]. These compounds



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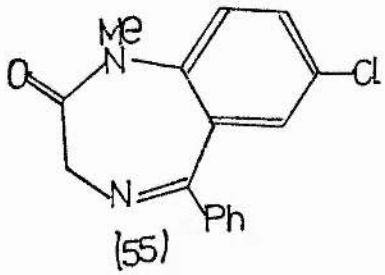


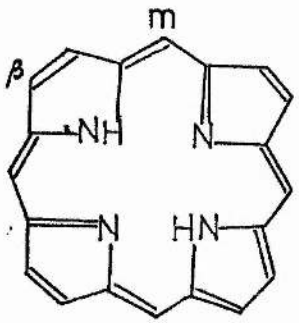
(55)

contain 1,9-diazanonatetraene systems and undergo electrophilic attack at the 7-position on nitration[149]. The 7-position may be preferred to the 9-position for steric reasons. ^{13}C N.m.r. studies of these compounds have not been reported.

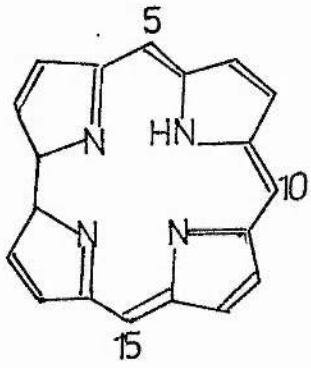
Benzo-1,5-diazepines[112] have been known since 1907[150] but the vinamidinium system in these compounds is perturbed by interaction with the benzene ring. Although their monocations

contain the vinamidinium system[150], in the case of the base the bis-imine tautomer is the predominant species and, the derived cation is stable over only a limited pH range[151]. They appear to lack meneidic character. Some of these benzo-1,5-diazepinium salts were prepared and their chemical behaviour with electrophiles has been investigated.

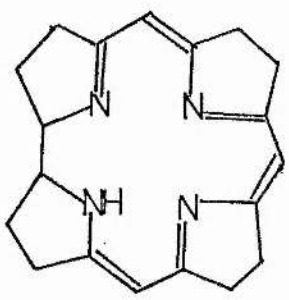
Perhaps the most important modified vinamidines are the corrin and porphyrin systems[152, 153], which occur in an enormous variety of natural products[154, 155]. Porphyrins (56) and their metal complexes are known to undergo electrophilic substitution at the meso (m) positions, although the β-position is said to be more active[156, 157]. Metal-free porphyrins may be deuteriated[158, 159], halogenated[160], and nitrated[157, 161], and the nitro-compounds may be reduced to an amine[157]. The corresponding complexes are deuteriated more readily than the bases[158], and can be formylated under Vilsmeier conditions[158]. A meso-thiocyanato derivative has been reported[162].



(56)



(57)



(58)

Tetrahydrocorrin systems(57) also shows resemblance to the dihydrodiazepines[163]. Complex salts of the former, for instance, undergo electrophilic attack at the 5, 10 or 15-positions. They can be halogenated, deuteriated or nitrated[163, 164]. The immediate substitution products, however, are unstable to oxidation[163, 164]. When the 5, 15-dibromo derivative is heated with chloroform in the presence of a trace of an acid, debromination occurs[163]. Di-debromination also takes place with nucleophiles, a mode of reaction similar to that found in the dihydrodiazepine series[25].

Little work appears to have been done on the reactions of corrins themselves with electrophiles. Similarly the reactions of electrophiles with simpler macrocycles[165, 166], prepared as possible model compounds for corrins and porphyrins, have not been studied. The synthesis and the reactions of some such compounds are reported in this thesis.

DISCUSSION

Part I

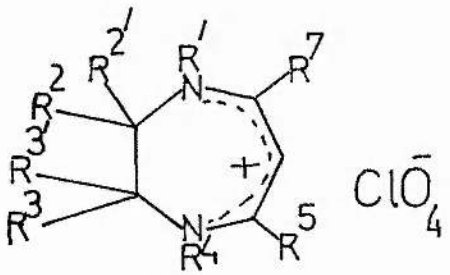
6-Aryldihydrodiazepines

Section 1

Preparation of Dihydrodiazepinium Salts and Open-chain Vinamidinium Salts

From β-Diketones

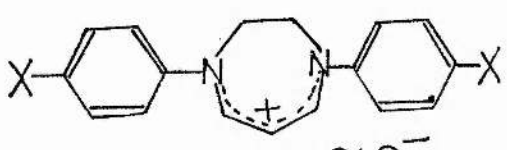
The common method of synthesis of dihydrodiazepines utilises the acid-catalysed condensation of 1,2-diamines with β-dicarbonyl compounds[53B]. The compounds (59a and 59b) were prepared in this way by warming the appropriate reactants in acid medium. These conditions favour the cyclisation and suppress the formation of the bisoxoenamine (40) as a possible alternative product[117,118,120]. Staab and co-workers earlier were able to isolate only the acetylacetone salt of C,C'-tetramethylethylenediamine when benzene was used as a solvent[116]. The present successful cyclisation, however, depends on presence of an acid-catalyst in the reaction medium. The 5,7-diphenyl analogue of the compound (59) was not isolated under these conditions, presumably because the aryl groups deactivate the keto groups of the β-diketone[113-115].



(59)

a, $R^1=R^4=H$, $R^{2'}=R^2=R^{3'}=R^3=R^5=R^7=Me$

b, $R^1=R^4=H$, $R^{2'}=R^2=R^{3'}=R^3=Me$, $R^5=R^7=Et$



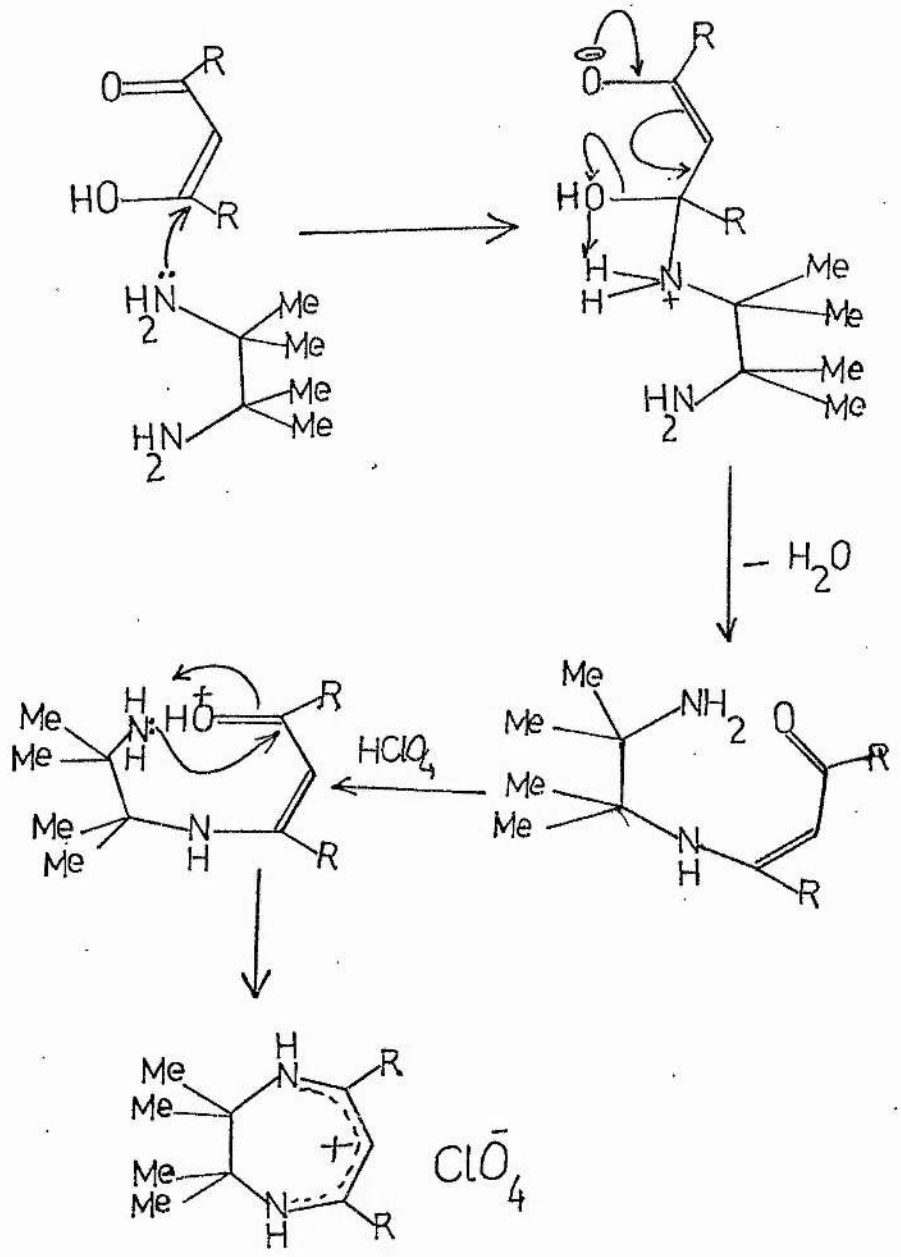
(60)

a, X=OMe

b, X=Me

c, X=Cl

Attack of the amine on the diketone may well involve the enol form of the latter as shown in Scheme 3.



Scheme 3

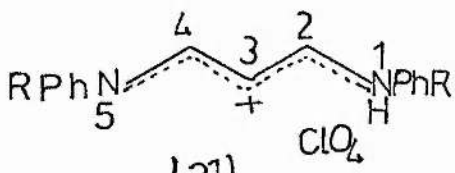
From Malondialdehyde Tetraacetals

Acetals of β-dicarbonyl compounds are converted into the dicarbonyl compounds in acid solutions, and under these conditions react readily with nucleophiles[28,52]. An N, N'-diphenyl-dihydrodiazepinium salt has been prepared[113] in a crude state

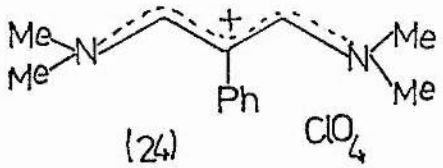
from the malondialdehyde tetraacetals, but purification of the product is difficult. The same method was used to obtain the compounds (60a-c) which were isolated in pure forms. N-N'-p-Disubstituted arylethylenediamines were prepared by reacting the appropriate p-substituted aniline with 1,2-dibromoethane.

From Vinamidinium Salts

Dihydrodiazepines may be prepared from derivatives of β-dicarbonyl compounds such as the vinamidinium salts, e.g. (21).

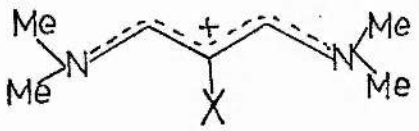


(21)



(24)

A synthesis of the 5,7-unsubstituted dihydrodiazepine from (21) was possible by the use of a high dilution method[167]. A similar method has led to the preparation of 6-aryl substituted dihydrodiazepinium salts (6-methyl analogues have been studied previously[112]). A 1,5-diaza-1,1,5,5-tetramethyl-3-phenyl pentadienium salt (24) had been recorded in the literature together with the 3-p-substituted arylvinamidinium salts (61a, b, e, h, and i)[18,73,74]. Some of the other vinamidinium salts (61c, d, f, g, j, and k) were prepared from the appropriately substituted aryl-acetic acids using the Vilsmeier formylating reagent. The key to the formylation of these substituted arylacetic acids is the fact that their methylene groups are reactive towards electrophiles. Acetonitrile will also react with dimethylformamide and phosphoryl chloride to give the corresponding vinamidinium salt[168].



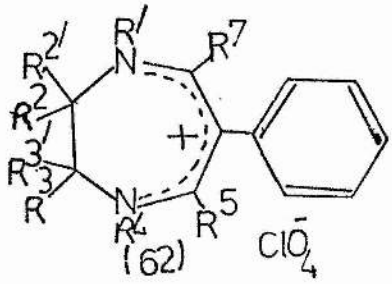
(61)

a, X=p-chlorophenyl
b, X=p-bromophenyl
c, X=p-methoxyphenyl
d, X=p-tolyl
e, X=p-nitrophenyl
f, X=o-tolyl
g, X=p-biphenyl
h, X=α-naphthyl
i, X=β-naphthyl
j, X=N-pyridyl
k, X=N-picolyl

Although some of these vinamidinium salts had been synthesised, their chemistry and, in particular, their behaviour with nucleophiles has been little explored.

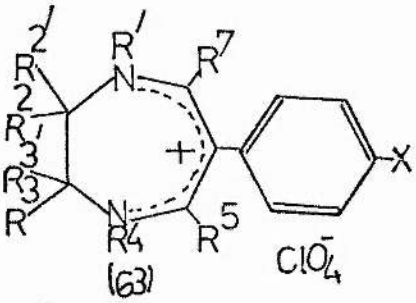
A methanolic solution of 1,2-diaminoethane reacts very readily with the 3-phenylvinamidinium perchlorate (24) to give the 6-phenyl dihydrodiazepinium perchlorate (62a). This is a special case of a transamination reaction, and a transformation of this type provides another example of the meneidic character of the 1,5-diazapentadienium system which is regenerated in the product.

The vinamidinium salt (24) possesses certain distinct advantages over the dianil salt (21) for preparations of the 6-aryl-diazepines. In the former case, the method of transamination is accomplished much more readily than in the latter. Also, use of the salt (24) obviates a technique of high dilution, and gives a cleaner product because the leaving dimethylamine is volatile whereas aniline, being involatile, may tend to be in equilibrium with the reactant ethylenediamine and thus retard the progress of cyclisation. Some idea of the versatility of this general method may be gained from the various dihydro-diazepines (62-70) which were synthesised by this method.



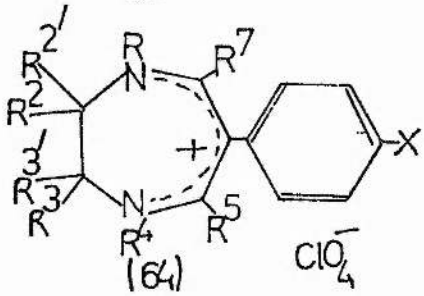
(62)

a, R^n=H
b, R^1=R^4=Me
c, R^1=Me
d, R^2=Me
e, R^2=$R^{2'}$=Me
f, R^1=R^4=CH_2Ph
g, R^2=R^3=cyclohexano



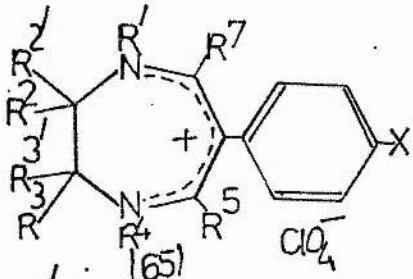
(63)

a, R^n=H
b, R^1=R^4=Me
c, R^1=Me
d, R^2=Me
e, R^2=R^3=cyclohexano
f, R^1=R^4=CH_2Ph
(X=Me in each case)



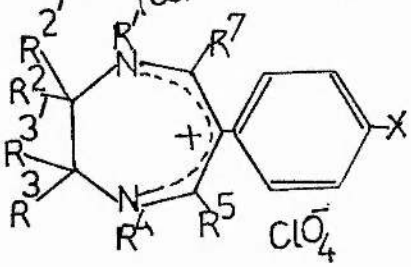
(64)

a, R^n=H
b, R^2=Me
c, R^2=$R^{2'}$=Me
d, R^1=R^4=CH_2Ph
(X=OMe in each case)



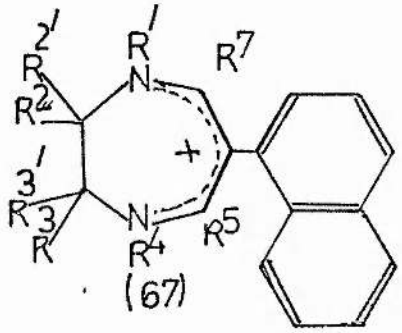
(65)

a, R^n=H
b, R^1=R^4=Me
c, R^1=R^4=CH_2Ph
(X=NO_2 in each case)



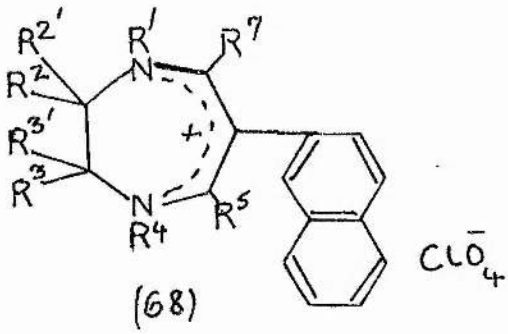
(66)

a, R^n=H, X=Cl
b, R^n=H, X=Br
c, R^n=H, X=Ph



(67)

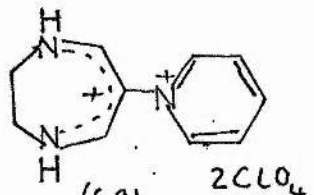
a, R^n=H
b, R^1=R^4=Me
c, R^1=Me
d, R^1=R^4=CH_2Ph



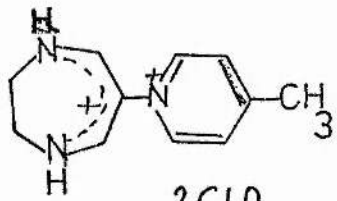
(68)

CLO_4^-

a, R^n=H
b, R^1=R^2=Me
c, R^1=Me
d, $R^{2'}$=R^2=Me
e, R^1=R^4=CH_2Ph
f, R^2=R^3=cyclohexano



(69) $2CLO_4$

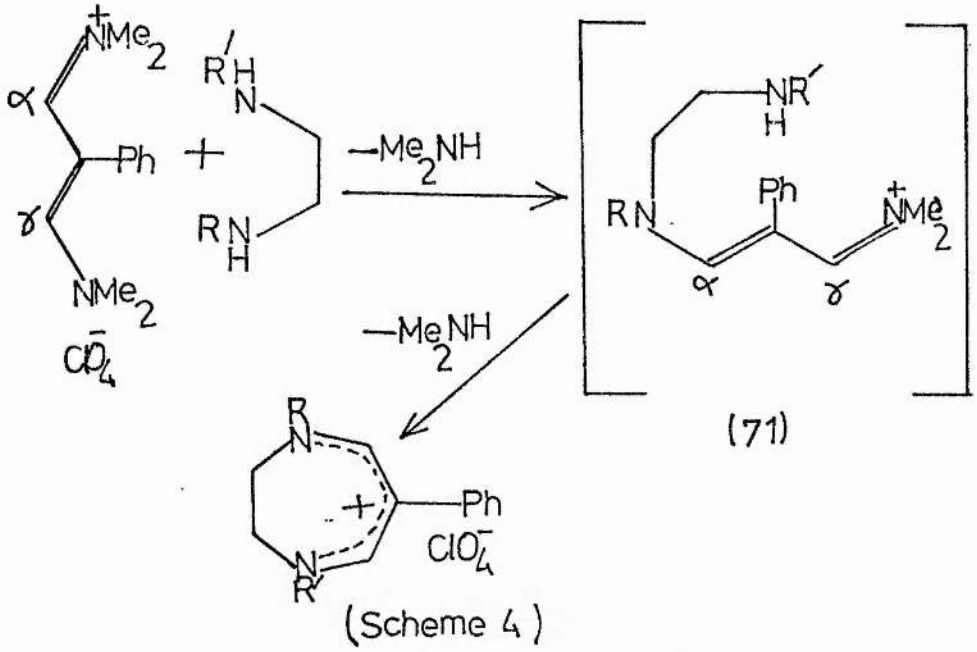


(70) $2CLO_4$

A series of 6-phenyl substituted dihydrodiazepinium salts (62a-g) was synthesised in over 80% yields by this general method. The biphenyl (66c) and the α-naphthyl analogues (67) were more difficult to obtain as solids than the corresponding β-naphthyl derivatives (68), although u.v. spectra indicated that in each case cyclisation required roughly the same time.

Steric factors may hinder or prevent cyclisation to give a dihydrodiazepinium salt, for example it had been shown previously that the 2,4-dimethyl derivative of (21) provided instead an imidazolinium salt[51]. Similarly, the vinamidinium salt (24) did not give the desired product with either N,N'-diethylethylenediamine or with C,C'-tetramethylethylenediamine. However, it proved possible to obtain the N,N'-dibenzyl derivative (62f). It is of interest to note that the 3-o-tolyl vinamidinium salt (61f) did not react with ethylenediamine; in this case the methyl substituent of the tolyl group may sterically prevent the vinamidinium chain from taking up the required conformation.

Formation of the dihydrodiazepinium salt must proceed in two steps, as shown in Scheme 4.



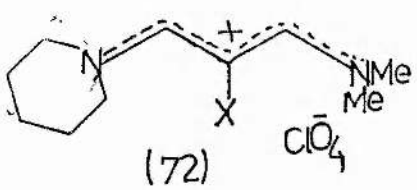
(Scheme 4)

Some evidence for this is provided by the studies of the reaction between the 3-aryl substituted open-chain vinamidinium salts and piperidine. The reaction of two equivalents of piperidine with one equivalent of either 3-phenyl , 3-p-tolyl , or 3-o-tolyl open-chain compounds (24, 61d, and 61f) in methanol only gave monopiperidine substituted products in each case (72a-c). In order to get the disubstituted piperidino analogues (73a-b) the use of a large excess of piperidine and a long reflux time were necessary. The o-tolyl open-chain compound, however, did not give the disubstituted product under similar conditions probably due to steric reasons.

One equivalent of either the 3-α-naphthyl (61h) or 3-β-naphthyl (61i) or 3-phenyl open-chain derivatives (24) gave disubstituted analogues (73a, c, d) with two equivalents of piperidine in

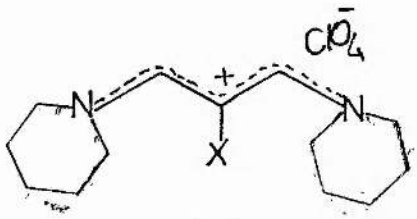
acetonitrile, but reaction required prolonged heating (ca 10 hrs) under reflux . It seems, thus, that the more polar solvents like acetonitrile might favour the formation of the disubstituted piperidino-compounds. It is emphasised, however, that the reactivity of these 3-aryl substituted open-chain vinamidinium salts is lowered compared with the similar reactions reported earlier for the 3-unsubstituted analogues[167] and the former require more severe reaction conditions. Earlier studies, which followed the reactions spectroscopically[167], have also indicated the existence of tight isosbestic point, thus showing the absence of an intermediate product.

It is apparent from this digression into the nucleophilic reactions of open-chain vinamidinium salts that the related cyclisation process must involve two steps in the reaction of the vinamidinium salts with ethylenediamine, and that the second condensation step is the rate determining step for these reactions.



(72)

a, X=phenyl
b, X=3-p-tolyl
c, X=3-o-tolyl



(73)

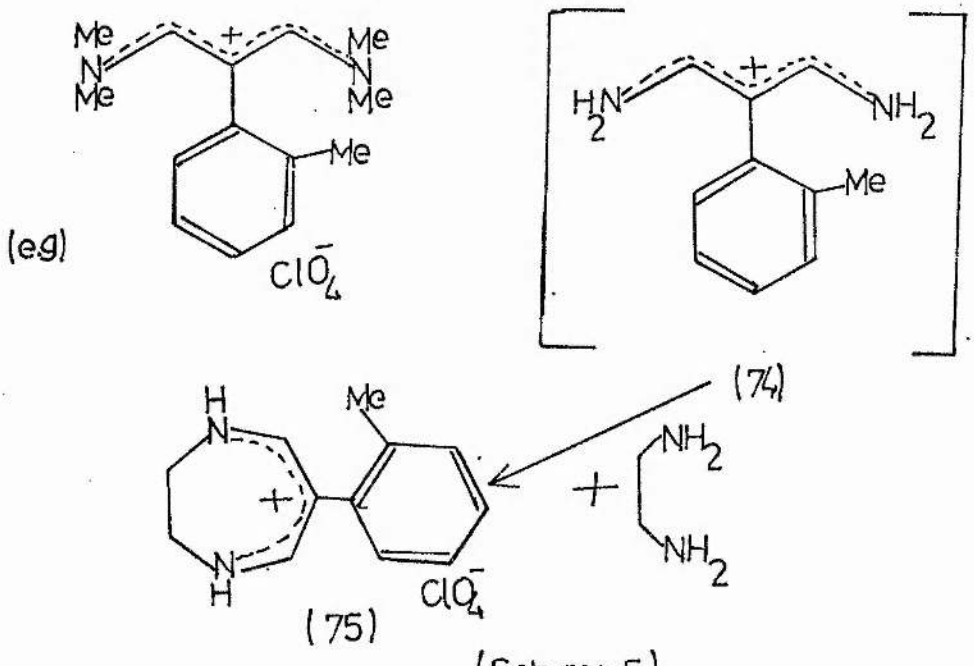
a, X=phenyl
b, X=p-tolyl
c, X=α-naphthyl
d, X=β-naphthyl

Of the other 6-phenyldihydrodiazepines, the 1,4,5,7-tetramethyl-6-phenyl and 5,7-dimethyl-6-phenyl derivatives still remain to be synthesised.

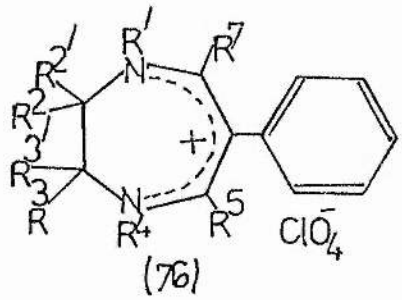
From Vinamidinium Salts by a 'One-Pot Ammonia' Method

Clearly, in order to synthesise the sterically crowded dihydrodiazepines (e.g. 75, and 76e) it was imperative to redesign or alter the reaction conditions. In one such attempt the higher boiling solvent, n-butanol, was used in place of methanol but only a partial cyclisation was observed, as indicated by u.v. spectroscopy.

Cyclisation to give such dihydrodiazepinium salts was accomplished by an alternative method - the 'ammonia method'. This method makes use of the principle that ammonia, because of its volatility, is an excellent physical leaving group. In this method, ammonia is first passed through a refluxing solution of the appropriate open-chain vinamidinium salt before adding the diamine to the reaction mixture. Ammonia displaces the dimethylamine to form a postulated intermediate (74), and in the next step ammonia is readily eliminated by the diamine (Scheme 5).

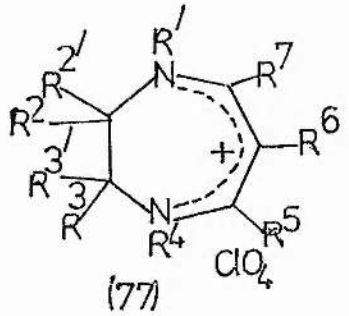


(Scheme 5)



(76)

a, R^n=H
b, R^1=R^4=Et
c, R^5=Me
d, R^1=R^5=Me
e, R^1=R^4=R^5=Me
f, $R^{2'}$=R^2=$R^{3'}$=R^3=Me



(77)

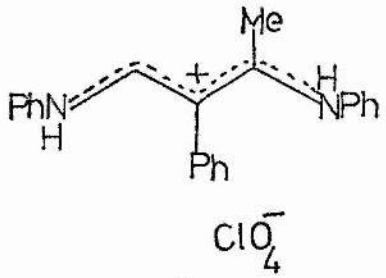
a, R^5=CH_2Ph, R^6=Me
b, $R^{2'}$=R^2=$R^{3'}$=R^3=Me
c, R^n=H

A wide range of dihydrodiazepinium salts (75-77) was synthesised in this way and displays the value of this general method.

From Vinamidinium Salts Formed from β -Chlorovinylaldehyde

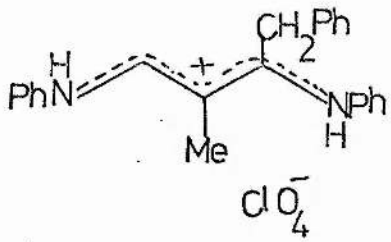
The vinamidinium salts (78-79) used for the preparations of the compounds (76c-e) and (77a) were themselves prepared by reacting aniline with substituted β -chlorovinylaldehydes in ethanolic perchloric acid. These β -chlorovinylaldehydes were readily accessible by the action of phosphoryl chloride and dimethylformamide on the appropriate α-methylene ketones, but using slightly improved conditions to the original procedure described earlier by Arnold and co-workers[66]. The formylation of the benzyl ethyl ketone gave an unexpected mixture of the compounds (80) and (81), but predominantly (80), although the benzyl methylene group had been expected to be the more reactive. This in turn provided the vinamidinium salt (79), which reacted with ethylenediamine to give a dihydrodiazepinium salt, whose ^1H n.m.r. spectrum showed it to have structure (77a) which requires

the assigned structures (79) and (80) of its precursors.



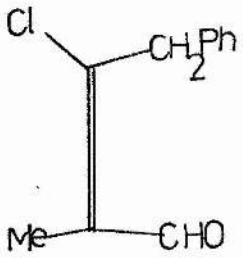
ClO_4^-

(78)

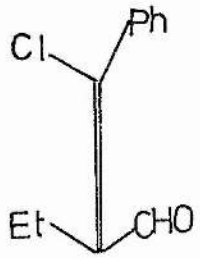


ClO_4^-

(79)



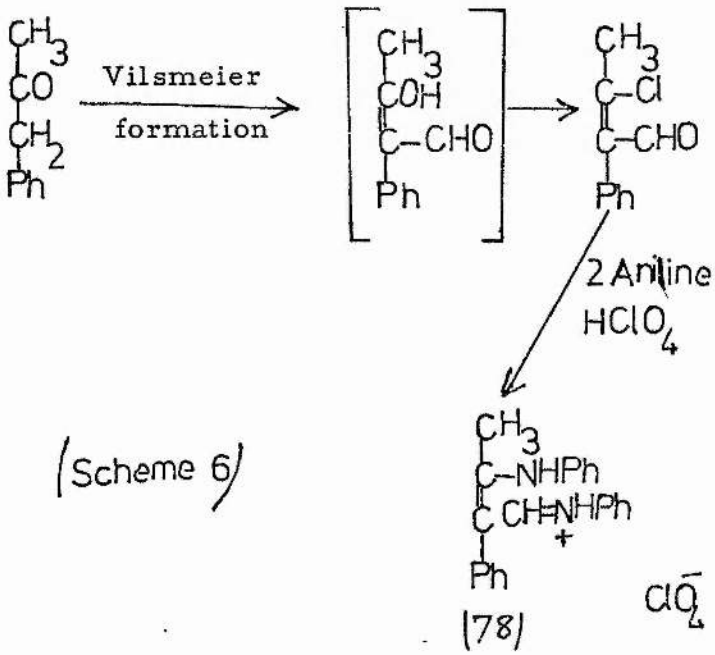
(80)



(81)

(for simplicity the alternative geometrical isomers of (80) and (81) are not drawn)

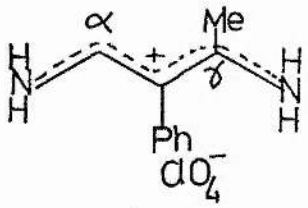
The scheme (6) outlines the overall method for the formation of the dianil salt (78).



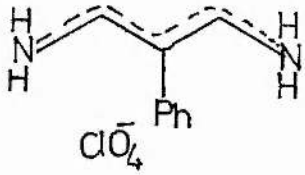
(Scheme 6)

(78)

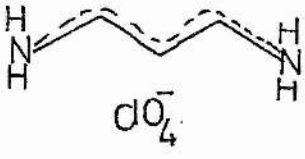
Isolation of the dihydrodiazepinium salts (75) and (76c-e) is of special interest because these compounds show steric resemblance to the $\underline{o}$-substituted biphenyl derivatives (see also section on electrophilic substitution). Moreover, the compound (76d) was formed rather than the isomeric 1,7-dimethyl-6-phenyl analogue. This is reasonable on the grounds of steric repulsion of the adjacent methyl substituents in the latter case. The isolation of the dihydrodiazepinium salt (76e) was surprising since an earlier attempted preparation of the 1,4,5-trimethyldihydrodiazepine derivative was unsuccessful[167]. Nevertheless, it does emphasise the value of the 'ammonia method' compared to the high dilution technique. When compound (78) is treated with ethylenediamine, there is no cyclisation but if it is treated with ammonia first the dihydrodiazepinium salt is formed. This implies again steric hindrance by the bulkier phenyl groups. The proposed intermediate formed from the dianil (78) by the 'ammonia method' is (82). It would be very interesting to isolate such an intermediate and study its chemistry but attempts to isolate (83) and (84) were unsuccessful. The picrate derivatives of these intermediates were also found to be too hygroscopic to isolate.



(82)



(83)



(84)

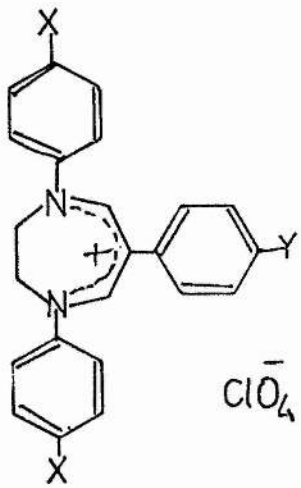
If it is accepted that the second-step determines the formation of diazepines, it seems possible that the initial attack

by the ethylenediamine (or N, N'-disubstituted ethylenediamine) on the intermediate (82) occurs at the site ɣ followed by attack at site α; were the attack the other way round cleavage to an imidazolinium salt might well result.

From arylmalondialdhydes

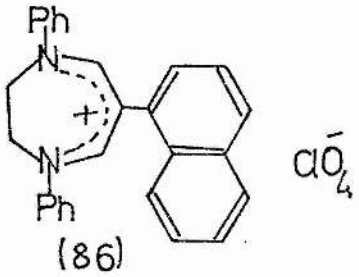
Despite the great versatility of the ammonia method it did not prove possible to prepare the N, N'-diphenylsubstituted 6-aryldihydrodiazepinium salts by this method. Vinamidinium salts such as (24) undergo alkaline hydrolysis to give the alkali salt of phenylmalondialdehyde. The derivatives (85a-e) were synthesised by liberating the free arylmalondialdehydes in situ from their sodium salts by the addition of methanolic perchloric acid, and by then adding the appropriately N-substituted diamines. The success of this method may be associated with the reactivity of the dialdehyde. The 1,4,6-triphenyldihydrodiazepinium salt (85a) has been previously recorded in the literature[86].

The salts (86) and (87) were also prepared in a similar way from sodium salts of substituted malondialdehydes.

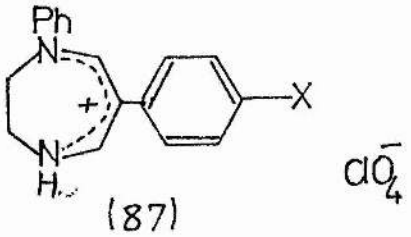


(85)

a, X=Y=H
b, X=OMe, Y=H
c, X=H, Y=OMe
d, X=Y=OMe
e, X=H, Y=NO_2



(86)



(87)

a, X=H

b, $X=NO_2$

Non-General Methods for the Preparation of Dihydrodiazepinium Salts

Transdiazepination

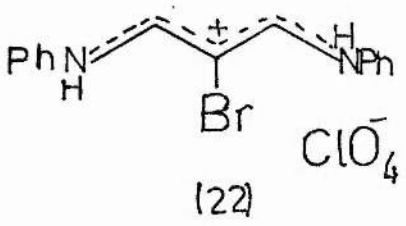
N,N'-Dialkylsubstituted dihydrodiazepinium salts were also prepared from the corresponding N-unsubstituted derivatives by treatment with an excess (tenfold) of disubstituted diamines. Thus the compounds (62b), (63b), (67b), (68b) and (88) were obtained from their respective N-unsubstituted analogues. The reverse reaction of these compounds with an excess of ethylenediamine did not take place, however, and the starting materials were recovered. This method is not a general method for preparing these salts; for example when the compound (62a) was heated under reflux with an excess of 1,2-diamino-2-methyl propane there was no transdiazepination, and only the starting material was recovered.

From Mucobromic Acid

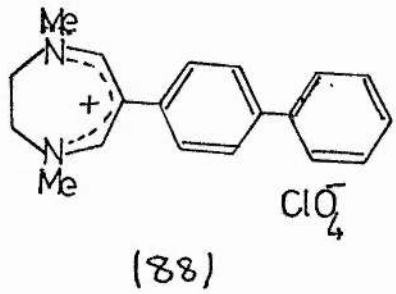
Another non-general method of synthesising 6-bromo- and 6-chloro-dihydrodiazepines is provided by the cyclisation of the intermediate (22), which is formed by the reaction of aniline

on mucobromic acid. Mucobromic and mucochloric acids are masked β -dicarbonyl compounds which yield (22) on reaction with aniline in ethanolic perchloric acid[56,57]

A careful nitration of mucobromic acid forms sodium nitromalondialdehyde monohydrate[169]. Attempted cyclisation of this compound with ethylenediamine in the presence of acetic acid to provide a 6-nitrodihydrodiazepinium salt resulted in an unidentified product which had m.p. 235-236°.



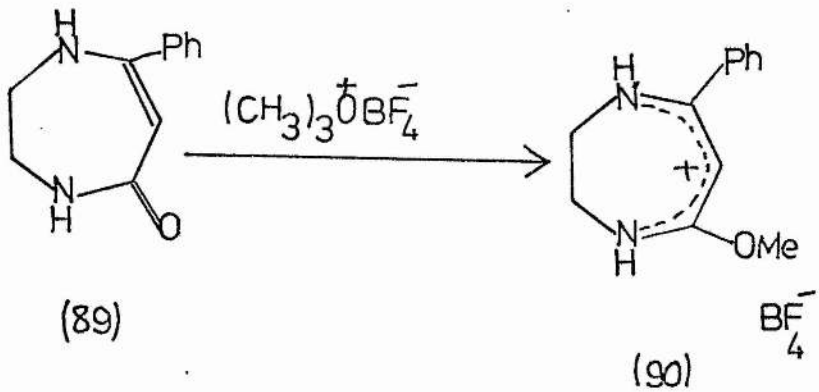
(22)



(88)

7-Phenyl-1,2,3,4-tetrahydro-1,4-diazepine-5-one (89)

5-Methoxy-7-phenyl dihydrodiazepinium fluoroborate (90) was obtained from the known 5-keto compound[170] (89) by methylating it with trimethyloxonium fluoroborate.



(89)

(90)

Attempted Preparations from Dichlorovinamidium Salts

2,4-Dichlorovinamidinium salts are very reactive intermediates for the preparation of a variety of heterocycles[44]. An attempted cyclisation of these salts to give dihydrodiazepines, using ethylenediamine, N,N'-dimethylethylenediamine, and dianilinoethane led only to the formation of the diamine salts. If an excess of the diamines was then added to this mixture there was tentative evidence from the u.v. spectra of the formation of 7-membered ring compounds which, however, could not be isolated. It is likely that work up may require anhydrous conditions.

Conclusion

It can be seen from the foregoing account that the open-chain vinamidinium salts have provided a valuable way of obtaining dihydrodiazepines. Their cyclisation to the 7-membered ring compounds is determined by the second-condensation step and may be controlled by steric factors in the open-chain molecule.

Section 2

General Properties of 6-Aryl-2,3-dihydro-1,4-diazepinium Salts and Investigations of Steric Factors Influencing these Properties

A systematic investigation of the properties of the completely unsubstituted dihydrodiazepinium salt has elucidated certain differences in properties from its related 5,7-substituted analogues. Such investigations prompted the synthesis of 6-phenyldihydrodiazepinium salt (62a). Although the latter compound has been reported earlier[86], its chemical properties remained unexplored.

The u.v. spectrum of (62a) shows a bathochromic shift of 22 nm (λ_{max} 352 nm) relative to the 6-unsubstituted analogue. The increased conjugation implies an overlap of the π-orbitals of the interacting functions. This suggests that the phenyl ring must be coplanar (or nearly so) with diazepine ring. This has an essential bearing on the properties of 6-aryldihydrodiazepinium cation.

The ^{1}H n.m.r. spectrum of the 6-phenyl-dihydrodiazepinium salt (62a) in trifluoroacetic acid (T.F.A.) as solvent shows the NH signals as broad peaks at low field. The NH protons are 'anchored' in T.F.A. and thus the protons at the 5(7)-position resonate as a doublet at low field (ca τ 2) and show a vicinal coupling constants $J_{1,7}(J_{4,5})$ of ca 8 Hz. The latter value has also been observed for the totally unsubstituted dihydrodiazepine. The 6-phenyl substituent, however, deshields the 5,7-protons slightly. The effect of vicinal NH coupling is also

evident in the resonances due to the methylene protons, and a typical complex multiplet is observed as for the unsubstituted derivatives[167].

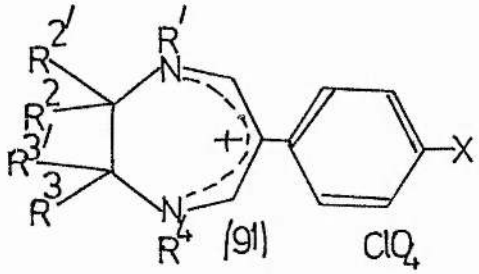
Deuteriation

The n.m.r. spectrum of the 6-phenyldihydrodiazepinium salt (62a) in deuteriated T.F.A. shows the disappearance of the NH protons which are readily exchanged, and thus the signals for the 5,7-protons and the methylene protons each appear as sharp singlets. This, thus, confirms the vicinal coupling between the methylene protons and NH, and of the 5,7-protons with the NH protons. There was no such exchange with deuteriated T.F.A. of benzene protons in 6-phenyldihydrodiazepine. After 20 days in this solution the compound (62a) showed no decomposition and the ratio of the 5,7-proton integral to that of the methylene and benzene protons remains unchanged, thus demonstrating the vanishingly low activity of these positions towards electrophiles[127]. Similar results have been observed earlier for the unsubstituted compounds[112].

Bromination

6-Unsubstituted dihydrodiazepinium cations are active towards electrophiles at the 6-position. It was interesting to find that the 6-phenyl substituted dihydrodiazepinium salt (62a) was also reactive towards such electrophiles. Although the cation (62a) remained unattacked by a deuteriated T.F.A., it was brominated with molecular bromine in methanol at room temperature. The ^{1}H n.m.r. spectrum reveals that attack by the bromine occurs on the phenyl ring at the p-position of the

6-phenyl substituted dihydrodiazepinium cation. This is apparent from the n.m.r. spectrum which shows an AA'BB' coupling pattern of the benzene protons. The vicinal coupling constant $J_{1,7}$ is again observed to be ca 8 Hz for the brominated compound (91a). Of the 6-phenyl substituted dihydrodiazepinium salts, the compounds (62h-e, 62g, and 76b) were also brominated to give (91b-g) using molecular bromine under the same conditions as (62a). In each case the bromine attack took place at the p-position of the 6-phenyl ring.

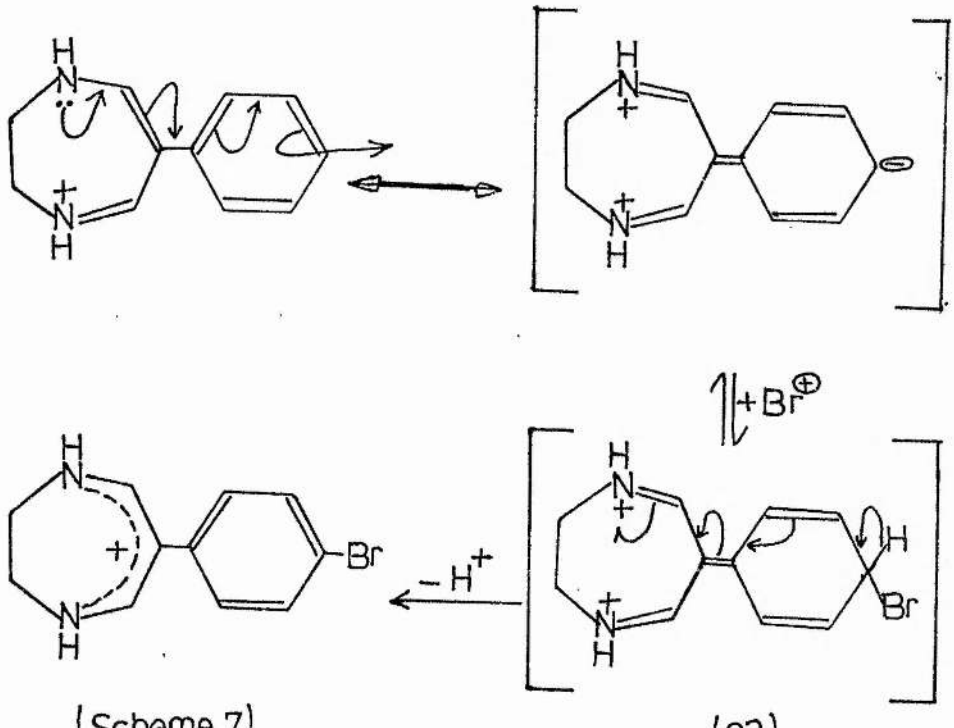


(91) ClO_4

(X=Br in each case)

a, R^n=H
b, R^1=R^4=Me
c, R^1=Me
d, R^2=Me
e, R^2=$R^{2'}$=Me
f, R^2=R^3=cyclohexano
g, R^1=R^4=Et

The following mechanisms (Scheme 7) may be invoked.



(Scheme 7)

(92)

The attack at the p-position of the phenyl ring by the bromine as an electrophile is intriguing and contrary to the usual assumption that a benzene ring which carries a positively charged substituent should be predominantly meta-substituted. However, a less naive approach shows that the dihydrodiazepinium cation is electron-rich and that the electron-releasing ability of the lone-pair on nitrogen should activate p- and o-positions of the benzene ring. The p-position is indeed more electron-rich compared with the m-positions (see ^{13}C n.m.r. section). o-Attack is unlikely on steric grounds (see later).

The mechanism for electrophilic substitution reaction involves an intermediate σ-complex (92), analogous to the Wheland intermediate in the electrophilic substitution of benzenoid compounds. This intermediate dication loses a proton to revert to the original mesomerically stabilised bromo-substituted product (in accord with the meneidic character of the system). Similar stable intermediate dication structures cannot be drawn for electrophilic attack at the 5- and 7-positions, and even 6-methyl-dihydrodiazepinium cation reacts preferentially at the 6-position rather than at the 5- or 7-position[112]. The resultant products from the latter compound are hydrolysis products since the dication intermediate has no mesomeric stabilisation and cannot gain such stabilisation by loss of proton, and, as a bisiminium salt, is readily hydrolysed. In the case of the 6-phenyl analogue the intermediate (92) can readily lose the p-proton to regenerate a stabilised molecule.

In contrast with the 6-phenyldihydrodiazepinium salt (62a), the 3-phenyl open-chain vinamidinium salt (24) remains unattacked by molecular bromine in methanol. This suggests that the rigid geometry of the vinamidinium system in the 7-membered ring compound may play an important role in electrophilic substitution.

The u.v. spectrum of 6-p-biphenyldihydrodiazepinium cation (66c) shows bathochromic shifts of 8 and 29 nm for its two peaks respectively relative to the compound (62a). This suggests that the two phenyl rings may be relatively coplanar with each other and with the diazepine ring. The biphenyl dihydrodiazepinium cation (66c) does not react with the bromine. This is not surprising since formation of a Wheland type intermediate would involve sacrifice of the resonance stabilisation energies of the dihydrodiazepinium system and of the biphenyl system.

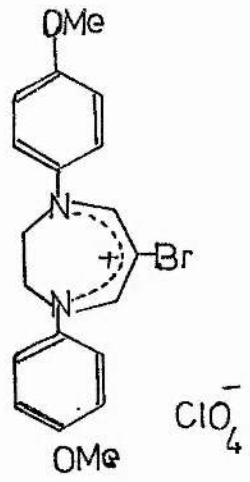
The 1,4-diphenyldihydrodiazepinium cation may undergo electrophilic substitution either at the 6-position or in the p-position of the N-phenyl ring. The 1,4,6-triphenyldihydrodiazepinium cation (85a) remained unattacked by an excess of bromine even after 7 days at room temperature. It is suggested that the reactive sites in this case might be in competition for the excess π-electrons thus diminishing their nucleophilicity, and/or that there may be steric factors involved. It is anomalous that the 1,6-diphenyl analogue (87a) also remained unattacked by the bromine. It was also surprising that the 1,4-dibenzyl-6-phenyldihydrodiazepine (62f) proved unreactive towards bromine whereas

both the 1,4-dimethyl- and 1,4-diethyl-6-phenyl analogues gave the p-bromophenyl derivatives (91b and 91g).

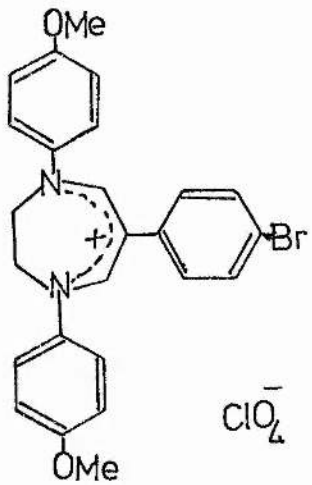
The 1,4-di-p-anisyldihydrodiazepinium salt (60a) undergoes electrophilic substitution at the 6-position, and only the monobrominated product (93) was isolated when this salt was treated with 3 equivalents of bromine. 1,4-Di-p-anisyl-6-phenyldihydrodiazepine (85b) gave the brominated product (94) presumably because two of the competitive reactive sites for electrophilic substitution are already occupied by the methoxy groups. However, 1,4-diphenyl-6-p-anisyldihydrodiazepine (85c) was unattacked by bromine.

The 6-p-anisyldihydrodiazepinium cation (64a) also did not react with the bromine. The preferred site of bromination for a 6-aryldihydrodiazepinium salt is blocked by the presence of the methoxy group. However this methoxy group is itself an activating group for electrophilic substitution, so that the benzene ring should be doubly activated. Reaction at the position ortho to the dihydrodiazepine ring is inhibited by steric factors but an alternative possibility was reaction at the position meta to the dihydrodiazepine ring since this position is activated by the p-methoxy group. That such reaction does not take place may be explained in that the required Wheland type intermediate would have two neighbouring positively charged systems, and it is not possible for the excess electrons of the dihydrodiazepinium system to interact conjugatively with the positively charged system in the benzene ring. Similarly, the 6-p-tolyldihydrodiazepinium cation (63a) was unattacked by bromine.

Thus, in essence it can be said that in a 6-aryl substituted



(93)



(94)

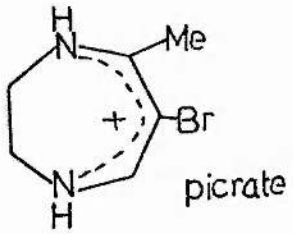
dihydrodiazepine, electrophilic attack in the aryl ring is influenced by the diazepine substituent, and that the usual directing effect of methoxy and methyl substituents is modified by the presence of the dihydrodiazepinium substituent. The 6-phenyl ring undergoes p-substitution, and this is associated with the coplanarity of the two rings.

The ^{1}H n.m.r. spectrum of the compound (63a) is of interest, for the benzene protons of this compound show a sharp singlet, thus, indicating an opposing effect of the two substituents. This signal is no longer a singlet when the N-atoms carry benzyl substituents as in (63f). The phenyl protons are also slightly deshielded in the compound (63f) compared with the compound (63a).

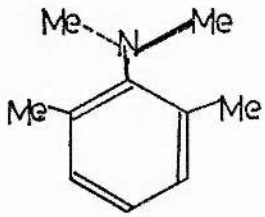
Neither the o-tolyldihydrodiazepinium cation (75) nor the 5-methyl-6-phenyldihydrodiazepinium salt (76c) reacted with bromine in methanol. It is probable that the methyl substiuent in both compounds (75) and (76c) twists the phenyl ring out of the plane of diazepine ring. Thus conjugation into the phenyl

is inhibited, and the requisite coplanarity of the Wheland intermediate (92) cannot be obtained. This idea is substantiated by the u.v. spectra. Each of the compounds (75) and (76c) shows a hypsochromic shift in its u.v. spectrum relative to the compound (62a), from λ_{max} 352 and 246 nm (ε7400 and 10900) (62a) to λ_{max} 347 and 238 nm (ε 9887 and 7217) (75) and λ_{max} 343 and 243 nm (ε 9707 and 7569) (76c) respectively. Further support for the lack of conjugative interaction between the rings comes from the ^{13}C n.m.r. spectra (see ^{13}C n.m.r. section) of these compounds.

In both of these methyl substituted analogues the electron density is reduced at the p-carbon of the 6-aryl substituent compared with 6-phenyldihydrodiazepine (62a) itself. Since both the compounds (62a) and 5-methyldihydrodiazepinium salt undergo electrophilic attack to give the bromo derivatives (91a) and (95), it is apparent that the near coplanar orientation of 6-phenyl ring is imperative for bromine attack.



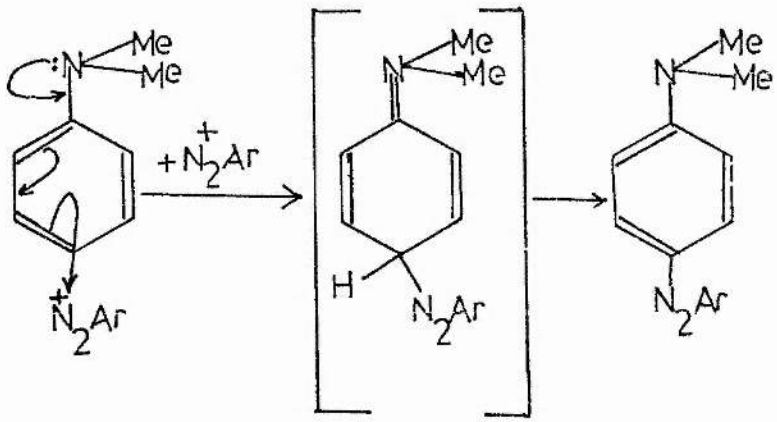
(95)



(96)

It is apparent that these results may be compared with observations for biphenyl and 2-methyl biphenyl, for instance, the latter shows a hypsochromic shift from 249 nm (ε19000) to 236.5 nm (ε10250)[171]. It is also interesting to compare these results with the original experiment by Friedlander[172]

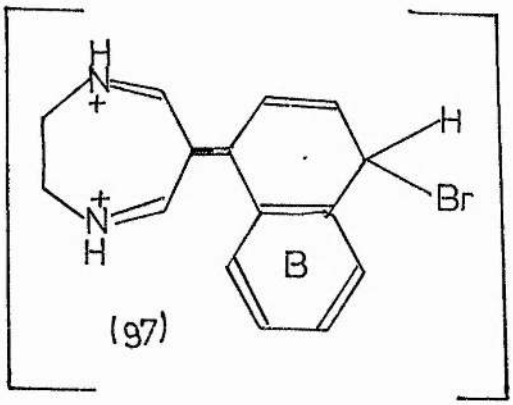
which shows that whereas N,N-dimethylaniline couples readily with diazonium compounds at the p-position, 2-methyl-N,N-dimethylaniline couples very slowly and 2,6-dimethyl-N,N-dimethylaniline does not couple at all. This is ascribed to the $-NMe_2$ substituent being forced by the vicinal methyl groups into a plane perpendicular to the benzene ring, viz. (96). The lone pair on the nitrogen is thus forced to be perpendicular to the benzene ring and thus cannot overlap with the π-electrons of the benzene ring as required in going to the transition state to the product as shown in Scheme 8.



(Scheme 8)

6-α- and 6-β-naphthyldihydrodiazepines (67a) and (68a) also underwent electrophilic substitution in the 6-aryl rings. Bromination seems most likely to occur at the 4-position (in the case of α-naphthyl derivative) since in the formation of the Wheland intermediate (97) the other benzene ring retains its benzenoid form and thus there is less loss of stabilisation than if reaction took place in the other ring (B) (See ^{13}C n.m.r. section).

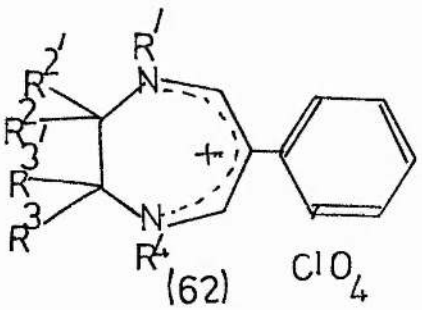
Reference to other naphthalene derivatives[173] with electron-donating 1-substituents indicates that C(4) is the normal site for further substitution.



(97)

Simple Bromination Kinetics

It is apparent that steric hindrance at the vicinity of the reactive sites plays a crucial part in the bromination of 6-aryl-dihydrodiazepinium salts. In an attempt to investigate the steric effects simple kinetics were carried out on the bromination of these diazepinium salts. The results are shown in Table 1.



(62) ClO_4

a, R^n=H
b, R^1=R^4=Me
c, R^1=Me
d, R^2=Me
e, R^2=$R^{2'}$=Me
g, R^2=R^3=cyclohexano

Table 1. Rates of Reaction of the Dihydrodiazepines (62) with Bromine in Methanol at 25°

Diazepinium Salts	62a	62g	62d	62b	62c	62e
Rate constants k (sec^{-1})	1.1×10^{-3}	1.2×10^{-4}	3.2×10^{-4}	2.1×10^{-5}	5.4×10^{-5}	7.0×10^{-5}

The kinetics and mechanisms of the substitution of the bromine have been studied in detail for the 5,7-dimethyl[131], 1,4,5,7-tetramethyl[129], and 5-methyl-7-phenyl[129] dihydrodiazepinium cations. In each case, second-order conditions in aqueous solutions were used, and the rate of reaction monitored by the potentiometric method developed by Bell[174].

Since under preparative conditions bromination was carried out in methanolic solution, the same solvent was used in this simple kinetic study. Phenyldihydrodiazepinium perchlorate concentrations were fixed at 0.2 M, while the bromine solutions were 0.02 M, and also 0.02 M in sodium bromide. The reactions were observed by conventional spectroscopic techniques, and in each case the decay of bromine absorption was followed at 460 nm; reactions were first order in $[Br_2]$ showing the presence of this species in the rate determining step. It is assumed that the bromine is consumed entirely by reaction with the dihydrodiazepinium cation in each case. It is emphasised that this investigation has no detailed mechanistic significance.

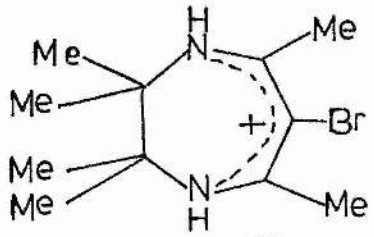
Methanol is a good solvent because of the relatively high solubility of a wide range of 6-phenyldihydrodiazepinium perchlorates, thus making it possible to study these compounds under identical pseudo-first order conditions. Methanol is also relatively less polar than, e.g., water and increases the selectivity of the reagents, and thus the sensitivity of the technique as a method of determining small differences in the reactivity of different dihydrodiazepinium salts is enhanced. A series of 6-phenyl-dihydrodiazepines studied for this purpose has relatively non-polar

substituents, and the rate of bromination in methanol is merely a probe of the steric factors of the dihydrodiazepines.

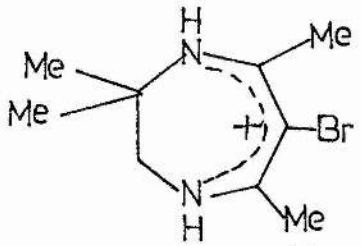
The simple experimental results (Table 1) indicated that the rate of bromination is fastest for 6-phenyldihydrodiazepinium perchlorate and slowest for the compound which carries dimethyl substituents at the 2-position with the rate for the monomethyl substituted analogue falling between these two compounds. The sp^3-hybridised part of the molecule undergoes inversion at room temperature, and if these rate constants are kinetically significant, it is inferred that it must be the axial methyl group of the compound (62e) which may be acting as a barrier to the incoming bromine molecules, thus inhibiting the reaction, especially since the results obtained for the derivative (62g), where the fused cyclohexano ring confers rigidity on the system and is equatorial, show that its rate of reaction is faster compared with (62e). These results show a parallel with those obtained earlier for the 6-unsubstituted dihydrodiazepinium analogues[167]. Hence, it is very intriguing indeed that the rate of reaction is affected considerably by a substituent at the 2-position which is 9 bonds away from the p-position of the phenyl ring.

If the methyl substituent at the 2-position is really acting as a barrier to incoming bromine molecules, it is possible that the initial bromine attack occurs at the nitrogen of the ring, which is adjacent to the 2-position. It is not unreasonable then to find the rate of reaction to be slower for the 1,4-substituted dihydrodiazepines than its N-unsubstituted analogue.

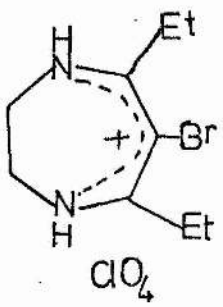
Although not studied kinetically, the bromination of 2,2',3,3',5,7-hexamethyl dihydrodiazepinium perchlorate (59a) is of interest because its brominated derivative (98) undergoes debromination after a short time when kept in solution (^{1}H n.m.r. evidence). No such debromination is observed for the compound (99). Thus the compound (98) may be used potentially as a brominating agent. It is noticeable again that the 2,2',3,3'-tetramethyl-5,7-diethyl dihydrodiazpine (59b) does not undergo electrophilic substitution whereas a stable 6-bromo analogue of the 5,7-diethyl dihydrodiazepinium cation (100) is formed which does not show debromination. The 2,2',3,3'-tetramethyl-6-phenyl compound (76f) only undergoes partial bromination with bromine in methanol.



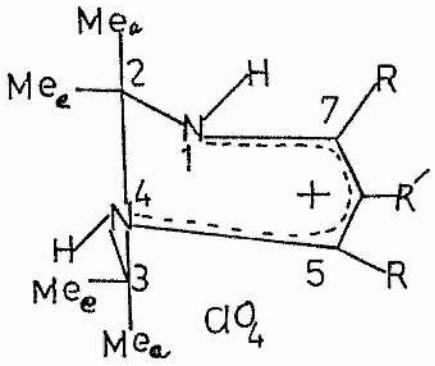
(98)



(99)



(100)



(101)

It is not very easy to rationalise these results but it is likely that with an increased crowding by a pair of axial methyl substituents (Me_a, 101) attack by bromine will be even more inhibited than with one axial methyl group at the 2-position. An increase in size of R (as in 101b) has been reported previously to slow the rate of reaction markedly[167]. It is, therefore, less surprising that compound (101b) does not undergo bromination. Also, if it is assumed that the bromine molecule forms a complex initially with the nitrogen of the vinamidinium system then it can be seen from (101) that this may be less probable with the axial methyl groups (Me_a) hindering approach to the nitrogen atom. It is also possible that these methyl substituents can cause crowding over the vinamidinium system (cf. 1,5-benzodiazepine section where in a boat conformation the 3-position methyl substituent is known to behave this way). It may also be noted that ^{13}C n.m.r. spectral data show a reduced electron density at the 6-position of (59a) compared with 2,2',3,3'-unsubstituted analogue (see ^{13}C n.m.r. section).

In conclusion, it is apparent that attack by bromine is sensitive to environment in the vicinity of the nitrogens of the heterocycle, and it is remarkable that such changes around that part of the molecule affect the p-position of 6-aryl ring.

Reactions with N-Halosuccinimides

Whereas 5,7-alkyl and aryl substituted dihydrodiazepines react with molecular bromine and with N-halosuccinimides at the 6-position to give 6-halogeno derivatives, the 5-methoxy-7-phenyl

(90) did not react with molecular bromine but was brominated with N-bromosuccinimide to form the 6-bromo derivative (102) This could be due to different mechanism, e.g., via radical formation. The following compounds (Table 2), which in addition were brominated by bromine, also formed halogeno derivatives with N-halosuccinimides.

Table 2. Halogeno Derivatives with N-Halosuccinimides in Glacial Acetic Acid

Compound	N-Bromosuccinimide	N-Iodosuccinimide	N-Chlorosuccinimide
62a	✓	✓	X
62c	✓	✓ (partial)	X
62d	✓	✓	X
62e	X	✓	——
62b	✓	X	——
62f	X	X	——
62g	X	X	——

✓, Halogenated product
X, Starting material recovered
——, Not attempted

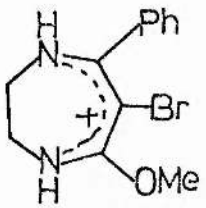
Nitration

The electron rich character of the 6-aryldihydrodiazepinium cation was further exemplified by the ready nitration of 6-phenyl dihydrodiazepinium salt (62a) using cold dilute nitric acid. Nitration, like bromination, occurred at the p-position of the phenyl ring (103). The ^{1}H n.m.r. spectrum of the compound (103) shows that the nitro group deshields the benzene protons and the AA'BB' doublet is interspersed with that of the 5,7-H signal.

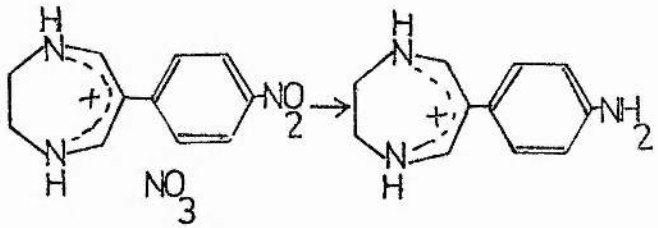
The reaction of 1,4-dimethyl dihydrodiazepinium cation (62b) with nitric acid under the same conditons, however, progressed a stage further, and p-nitrobenzoic acid was isolated. Nitration is presumably followed by acid hydrolysis to give p-nitrophenyl-malondialdehyde which is in turn oxidised and decarboxylated to provide the final product. Nitration must have occurred prior to hydrolysis and oxidation because otherwise m-nitrobenzoic acid would be formed predominantly. Similar results were obtained for the compounds (62c-d).

Nitration of the open-chain 3-phenylvinamidinium salt (24) also gave p-nitrobenzoic acid.

The nitro group of the compound (103), like nitro derivatives of benzenoid compounds, could be reduced to an amine. Also, like arylamines the resultant amine could be acylated with a mixture of acetic anhydride and acetic acid.



(102)



(103) (104)

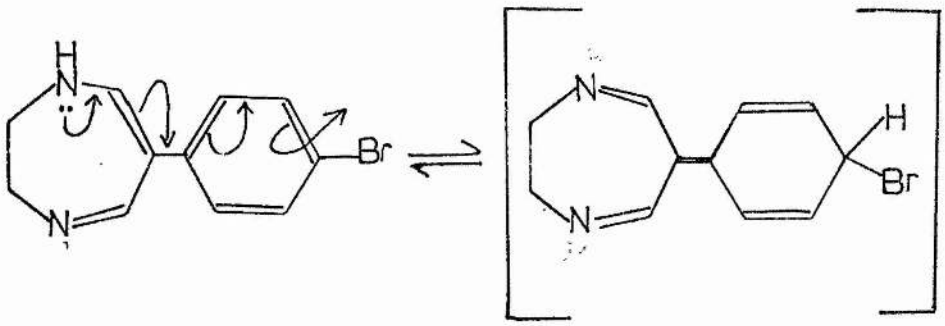
Compound (104) showed absorption maxima in the u.v. spectrum of 325 and 270 nm with hypsochromic shifts to 300 and 240 nm on addition of dil. H_2SO_4, which was reversible in alkali. Compound (104) was also diazotised with sodium nitrite and fluoroboric acid. Attempted diazo coupling of the compound (62a) with

p-nitrophenyldiazonium chloride was unsuccessful, and so was attempted methylation using methyl fluorosulphonate. Although one reduction of (103) to (104) proceeded successfully, attempted repetitions of this reaction proved to be unsuccessful.

Reaction with Nucleophiles

Unlike the 5,7-dimethyldihydrodiazepinium salt, the 6-phenyldihydrodiazepinium cation (62a) reacted with an excess of N,N'-dimethylethylenediamine, and the corresponding 1,4-dimethyl substituted derivative was obtained in reasonable yield. The salts (62b, 63b, 67b, 68b and 88) were also prepared by this method from their corresponding 1,4-unsubstituted dihydrodiazepinium salts. This transdiazepination reaction however, is not of general synthetic utility, for an attempt to prepare the 2,2-dimethyl derivative from 1,2-diamino-2-methyl-propane and the salt (62a) was unsuccessful. This chemical behaviour is similar to that of the totally unsubstituted dihydro-diazepines, and demonstrates the electrophilicity of the 5- and 7-positions of the ring. It is likely that transdiazepination takes place in a two step process like the cyclisation of the open-chain vinamidinium salts with the diamines. It also seems likely that transdiazepination process is sensitive to steric factors because the compound (62b) remained unattacked when heated for 12 hrs with an excess of ethylenediamine. Similarly, no reaction took place between the 5-methyl-6-phenyldihydro-diazepine (76c) and an excess of N,N'-dimethylethylenediamine. Reaction of a large excess of piperidine with compound (62a) gave a mixture of unidentified products.

Whereas the 6-bromo-5,7-dimethyldihydrodiazepinium salt reacts readily with nucleophiles with replacement of the bromine, the 6-p-bromophenyldihydrodiazepinium salt (91a) does not undergo a substitution reaction with methoxide ion. This may be rationalised in terms of the proposed mechanisms of these reactions (Scheme 1), which is thought to involve the bis-imine tautomer of the heterocycle. The formation of such a tautomer (Scheme 9) must be suppressed because of the loss of resonance stabilisation energy which in the case of the phenyl substituted analogue is high, since resonance energies of both the dihydrodiazepinium and benzene moieties will be lost.



Scheme 9

The 6-bromo-5,7-dimethyldihydrodiazepinium salt reacts with thiourea by an unusual substitution to give the 6-unsubstituted compound (Scheme 1). However, there was no reaction between the compound (66b) and thiourea in methanol.

Hydrolysis

Whereas the totally unsubstituted dihydrodiazepinium cation is hydrolysed irreversibly by mineral acids, the 6-phenyldihydrodiazepinium salt (62a) was resistant to acid (conc. HCl) hydrolysis but formed the sodium salt of phenylmalondialdehyde on alkaline hydrolysis; the 6-α-naphthyl derivative was similarly hydrolysed. The conversion of the dihydrodiazepinium salt into its base by the alkali, and then possibly the formation of the bis-imine tautomer may facilitate the ring opening to form the appropriate malondialdehyde.

When the bromo-derivative of 6-α-naphthyldihydrodiazepinium salt was hydrolysed in the presence of potassium permanganate in order to oxidise the possible naphthylmalondialdehyde derivative to its acid, in an attempt to identify the position of the bromine in the naphthyl ring, only polymeric material was obtained.

Free Radical Formation

The 6-phenyldihydrodiazepinium salt (62a) gives a blue solution with conc. sulphuric acid. This is thought to be due to formation of a free radical, which was detected by E.S.R. spectroscopy. It is likely that the formation of this free radical is associated with the presence of the phenyl ring in this compound, because no such radical has been detected from the 6-unsubstituted dihydrodiazepines. The radical may be oxygen sensitive but no further investigations were carried out. However, the E.S.R. spectrum shows the presence of this radical even after 24 hrs,

and thus it is very stable. The blue colouration also seems to persist for nearly 4 days. The u.v. spectrum of the compound (62a) in conc. sulphuric acid taken after 24 hrs was identical to that of the fresh sample, and it showed a hypsochromic shift from 352 to 347 nm and a bathochromic shift from 246 to 278 nm (ref. conc. H_2SO_4). The same sample showed λ_{max} values of 350 and 260 nm (in methanol) and 349 and 252 nm (in water). However, the recovered solid had λ_{max} peaks at 352 and 257 nm. Thus, these results imply that the phenyl group is involved as well as the conjugated system of the diazepine ring.

The ^1H n.m.r. spectrum of the compound (62a) in D_2SO_4. showed the broadening of the signals in the aromatic region and also around τ 6.0 after ca 45 mins, and a total disappearance of the proton signals in the aromatic region after ca 75 mins.

The formation of a blue colour in conc. H_2SO_4 seems to be a common feature of 6-aryl substituted dihydrodiazepinium cations, for the u.v. spectrum of the compound (63a) in sulphuric acid also showed λ_{max} shifts from 358 and 248 nm to 340, 290 (shoulder) and 255 nm (in methanol).

Electronic Spectra

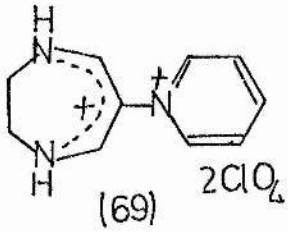
The substituent effects on the position of the absorption maxima in 6-aryldihydrodiazepinium cations show general trends. Thus methyl groups at 1- and 1,4-positions cause bathochromic shifts of +11 and +15 nm in the 'diazepine region' of the spectrum and +5 and +7 nm in the 'aryl region', with respect to the reference compound (62a) whereas a bathochromic shift of +20 nm is observed in the 'diazepine region' with benzyl

substituents at the 1- and 4-positions. There is also an increase in the intensity of absorption. A methyl substituent at the 5-position causes hypsochromic shifts of -9 and -3 nm, and a corresponding diminished intensity of absorption. Each phenyl substituent at 1,4-positions causes a bathochromic shifts of +22 nm. This general situation shows some parallel with the absorption maxima of azulenes in that méthyl substituents at centres of high π-electron density produce bathochromic effects while methyl substituents at centres of low π-electron density produce hypsochromic effects.

Methyl substituent at the p-position of the 6-phenyl ring causes bathochromic shifts of +6 and +2 nm relative to the compound (62a) whereas an o-substituted methyl group produced hypsochromic shifts of -5 and -8 nm; the p-methoxy substituent causes bathochromic shifts of +10 and +2 nm. Different halogen substituents at the p-position to the 6-phenyl ring also alter the value of absorption maxima.

The 6-N-pyridyldihydrodiazepinium dication (69) does not react with either elemental bromine or with N-bromosuccinimide. However, its u.v. spectra in various solvents are of interest.

Spectroscopic evidence (n.m.r. as well as u.v.) shows that either a mono- or a di-cation may be formed, depending upon the pH of the solution. The monocation form, however, could not be isolated in pure form. On addition of methanolic potassium hydroxide to (105) further spectroscopic changes occur and a coloured species is formed which may be the pyridinium ylide (106). This new species is however very unstable and



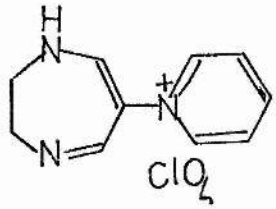
(69)

Colourless
Soluble in H_2O

λ_{max} (MeOH)

340 nm (shoulder)
328 nm
268 nm

+ $HClO_4$

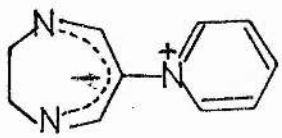


(105)

Pale Yellow
Insoluble in H_2O - can be isolated

λ_{max} (MeOH)

355 nm (shoulder)
322 nm
265 nm



(106)

Possibly generated in situ with 2 moles of KOH in MeOH

attempts to isolate it provided only polymeric material. Attempts to trap the ylide by reaction with 2,4-dinitrobenzaldehyde also only gave polymeric products.

Conclusion

It is apparent from a brief survey of the general properties of 6-aryldihydrodiazepinium salts that they show resemblance to activated benzenoid compounds like aniline and phenol. For example, both the nitration and bromination are accomplished

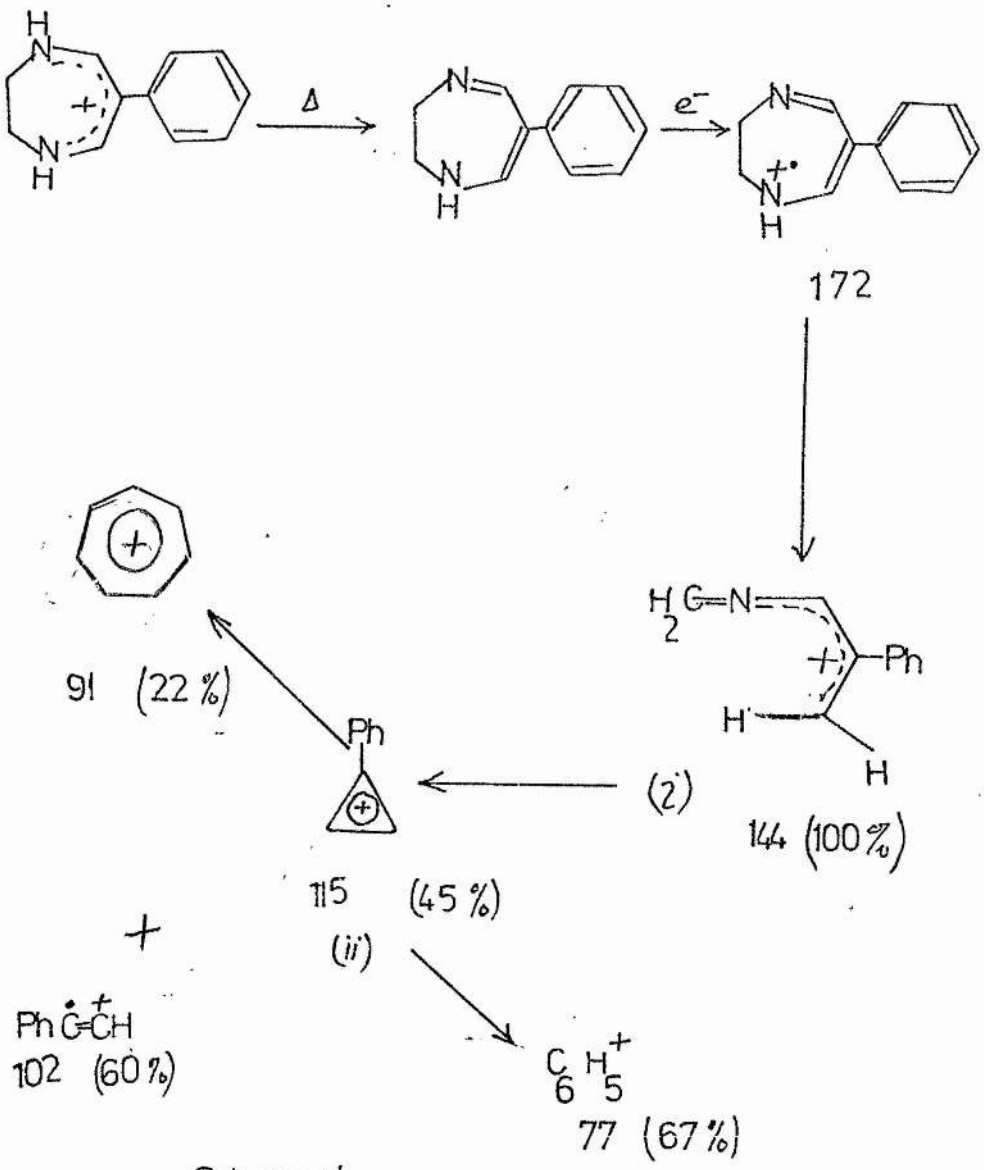
either at room temperature or below. The activation of the 6-phenyl ring is an important consequence of the stabilised electron-rich vinamidinium system of the dihydrodiazepine ring, and the fact that there is an important and effective conjugative electron donation into the phenyl ring. The conjugative interaction between the two rings, however, is determined by the orientation of the phenyl ring with respect to the vinamidinium system. This orientation is sensitive to steric factors, and obviously plays a central role in the chemistry of these dihydrodiazepines.

Section 3

The mass spectra of 6-aryl-2,3-dihydro-1,4-diazepinium salts

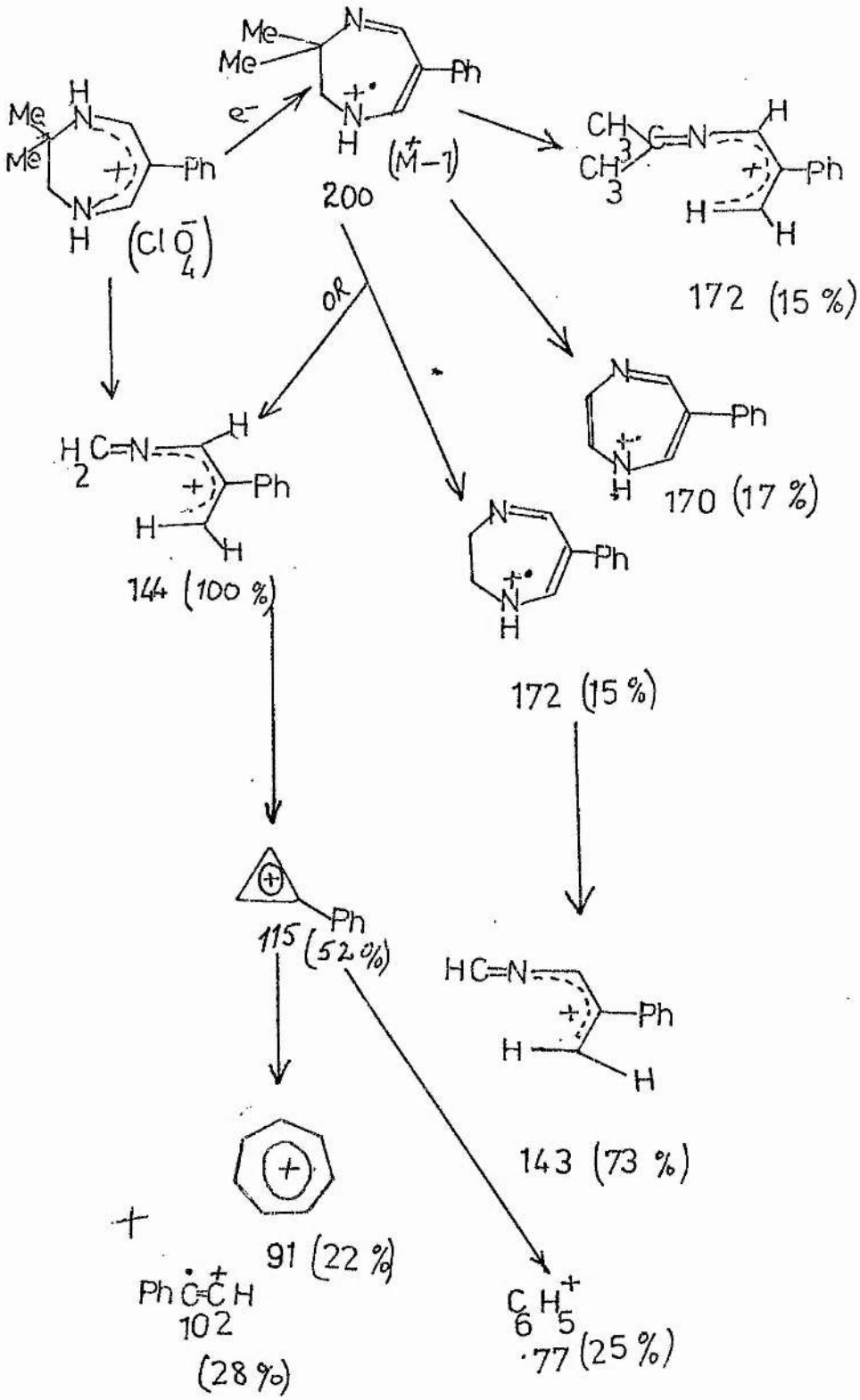
Staab and Wünsche[200] had earlier reported the breakdown patterns of a selection of 2,3-diaryl-1,4-diazepine derivatives. Recently[182], mass spectral studies of 2,3-dihydrodiazepinium salts have been recorded. The present work provides the first examples of such studies for the 5,7-unsubstituted dihydrodiazepines. The 6-aryldihydrodiazepinium salts, like the 6-unsubstituted analogues, showed, in general, peaks of low-intensity at m/e corresponding to the molecular ion of the cation, but this is most likely to be the ^{13}C-isotope peak of the free base. In that case, thermal dissociation of the salt, where possible, would appear to precede electron bombardment.

For 6-aryl substituted dihydrodiazepinium salts, like the 6-unsubstituted derivatives, the most intense peak of the molecular ion cluster, is usually that of the base with the exception of the 5-methyl-6-phenyl derivative and the 2,2,3,3-tetramethyldihydrodiazepinium iodide where the "true" molecular ion peaks at 187 (73%) and 153 (85%) were obtained respectively. Thus these are the first examples where the mass spectra of N,N'-unsubstituted dihydrodiazepinium salts give the "true" molecular ion peaks. The chief fragmentation process, confirmed by the presence of metastable peaks, was the elimination of the N^1-C^2 fragment, leaving a positively charged linear compound (i) (Scheme i). Further decomposition of (i) resulted in the formation of (ii), hydrogen cyanide and tropylium ion.

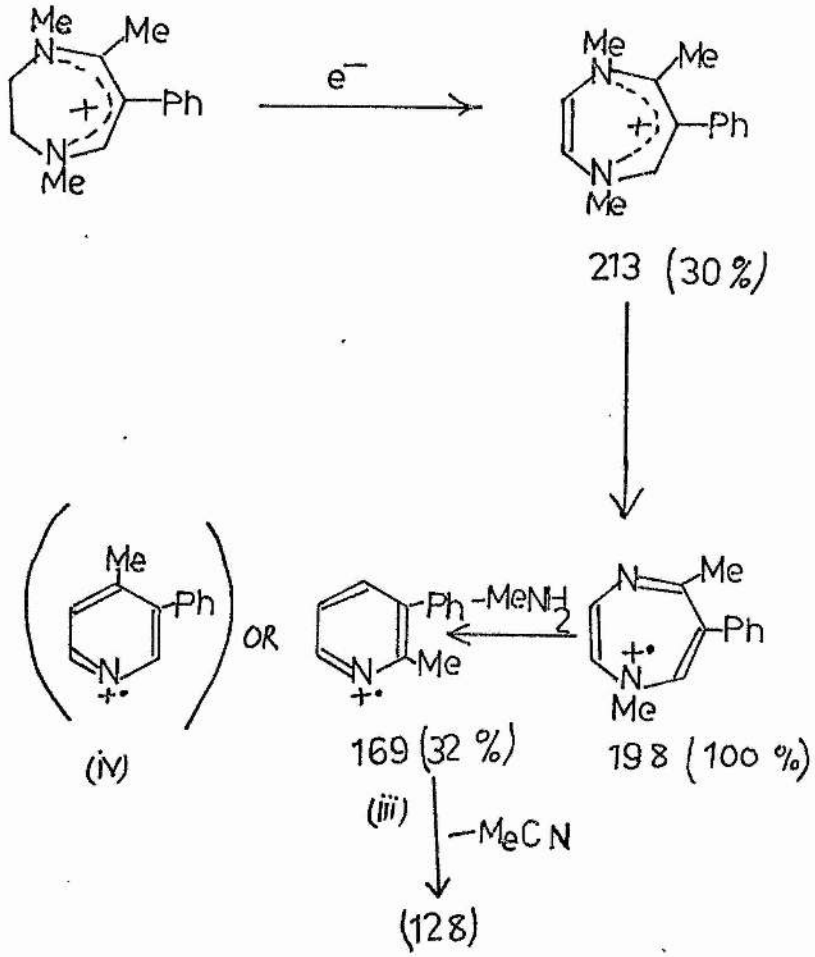


Scheme (i)

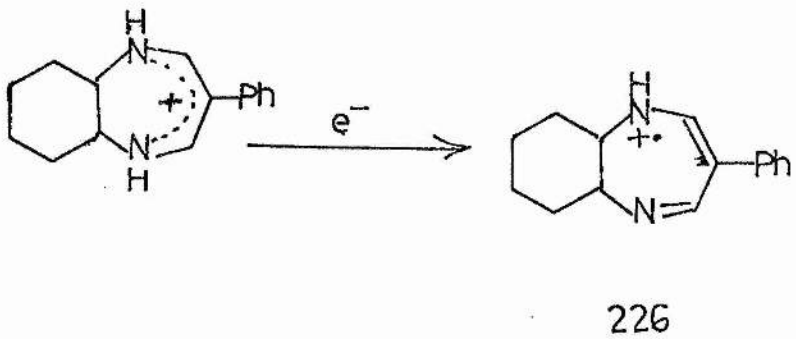
It has been shown[182] that 2,2-dimethyldihydrodiazepinium salts exclusively lose the radical $Me_2C{=}N\cdot$ in preference to $H_2C{=}N\cdot$, while for the N-methyl derivatives it is the loss of $H_2C{=}N\cdot$ which has preference over $H_2C{=}\dot{N}Me$. Likewise, in the case of 2,2-dimethyl-6-aryl substituted analogues the loss of the more highly substituted $R_2C{=}N\cdot$ dominates; the fragmentation patterns are shown in Scheme (ii).


Me
Me
Ph
e⁻
(M⁺-1)
200
(ClO₄⁻)
172 (15 %)
OR
170 (17 %)
144 (100 %)
172 (15 %)
115 (52 %)
143 (73 %)
91 (22 %)
102 (28 %)
77 (25 %)

Scheme (ii)



Scheme (iii)



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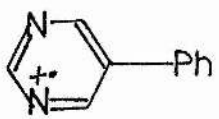


156 (45 %)

(V)

The fragmentation pattern of 1,4,5-trimethyl-6-phenyl-dihydrodiazepinium salt is very interesting, for it confirms very nicely that the first methyl group lost is as shown in Scheme (iii). Two pyridines (iii) and (iv) could result from the loss of $MeNH_2$, but only the former (iii) could subsequently lose MeCN.

Since the usual primary decomposition process involves the breaking of the C^2-C^3 bond, this mechanism cannot proceed in the same way in the case of the 2,3-cyclohexano-6-phenyldihydro-diazepinium salt. Instead, this compound shows an intense peak at m/e 156, which probably corresponds to the formation of the pyrimidinium cation (V). A similar result has been recorded for the 5,7-dimethyl and 5,7-diphenyl-6-unsubstituted analogues[182].

DISCUSSION

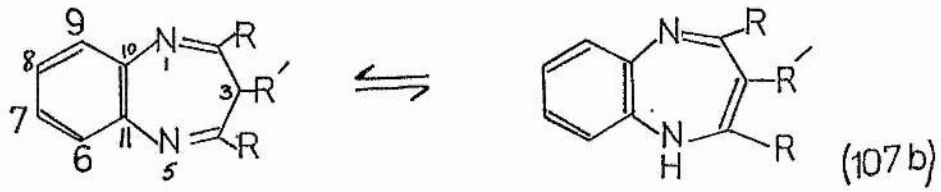
Part II

1,5-Benzodiazepines

Introduction

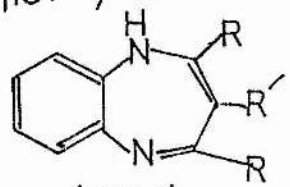
1,5-Benzodiazepines (107a) are the 2,3-benzo-fused analogues of the 2,3-dihydro-1,4-diazepines. 1,5-Benzodiazepines, which have been known since 1907[150], could also, like the dihydrodiazepines, exist potentially in tautomeric forms (107a,b,c). However, the bis-imine tautomer (107a) is the predominant species for these compounds. This is thus in direct contrast with their dihydrodiazepine counterparts. In form (107a) some extra stabilisation is achieved by conjugation of the anil groups with the benzene ring. Cyclic conjugation as in form (107b) may destabilise the molecule since it involves either interaction of 8π-electrons around the seven-membered ring or, in canonical form (107d), of 12 π-electrons around the periphery of the molecule; either of these formalizations are counter-Hückel systems[5].

Protonation of benzodiazepines leads to the formation of the monocation (107e) and the dication (107f). The bases and dications of 1,5-benzodiazepines are normally colourless (probably due to loss of the conjugated system in the ring) whereas the monocations are intensely coloured, frequently dark purple. The pKa value for the base to monocation equilibrium of a 1,5-benzodiazcpine has been determined as 4.5 (2,4-dimethyl, (108), potentiometric)[53B] and 5.76 (2,4-dimethyl, soectroscopic)[175]. The presence of 2,4-diphenyl groups lowers the basicity still further[175]. The pKa

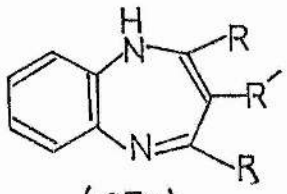


(Bisimine)
(107a)

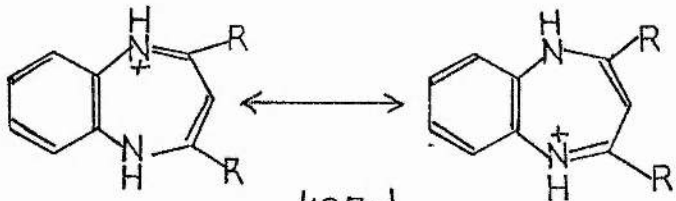
Conjugated form
(107b)



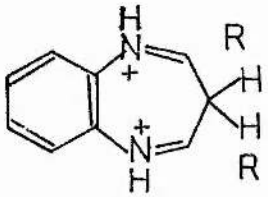
(107d)



(107c)



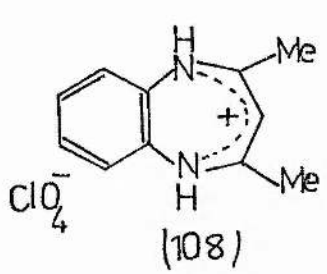
(107e)



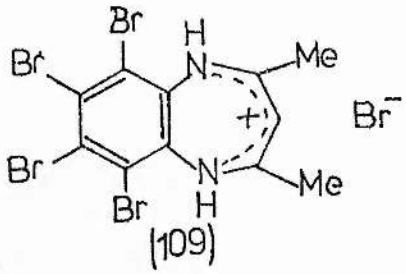
(107f)

value for the monocation to dication equilibrium is ca -1. Although the benzodiazepinium cation contains a vinamidinium system, it is the preferred system only over a moderate pH range. It is more easily hydrolysed than the dihydrodiazepine counterparts[176]. The low basicity of benzodiazepines is associated with their less stabilised cations, with the interaction between the amine groups and the benzene ring, and also with the necessity for tautomeric

change of the base to less favoured conjugated form on cation formation.



(108)



(109)

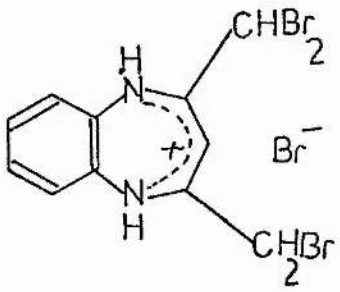
Recently, x-ray crystallographic analyses[177] have shown that the lengths of the N-C bonds imply that there is only limited cross-conjugation between the π-bond systems to the right and left of the molecule.

Electrophilic Substitution Reactions - Bromination

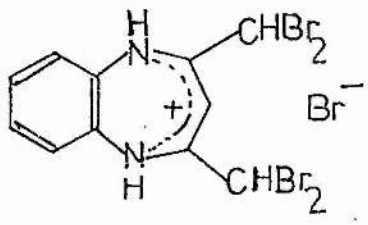
There are several important differences between the dihydrodiazepines and 1,5-benzodiazepines and these have been reviewed more comprehensively elsewhere[178]. One of the distinguishing features is the lack of meneidic character in the vinamidinium system which 1,5-benzodiazepines exhibit, which is exemplified by their unpredictable behaviour with electrophiles. Indeed, it was this behaviour which led to the re-examination of some of the properties of these types of compounds.

Earlier reports[151] on the bromination of (108) suggested that this compound with an excess of bromine in glacial acetic acid yields a tetrabromo derivative (109). More recently, R.L. Williams and his co-workers[179] suggested an alternative structure (110) for the tetrabrominated product. Hence, a more extensive study of the chemistry of these compounds was undertaken.

The reaction of compound (108) with one equivalent of bromine in acetic acid gave the unbrominated compound (108) as its bromide salt. The absence of a perchlorate ion (band in the I.R. spectrum) confirmed the anion exchange. When four equivalents of bromine were used, the best structure which could be assigned to the isolated product was (110) from evidence provided by its ^{1}H n.m.r. spectrum (see Table 4). However, with the use of six equivalents of bromine 2,4-bis(dibromomethyl)-1,5-benzodiazepinium bromide (111) was obtained. These structures are based on the absence of methyl signals in the ^{1}H n.m.r. (see Table 4). Hence, it appears that the initial anionic exchange takes place before the bromine is consumed as an electrophile to give the brominated benzodiazepines.



(110)

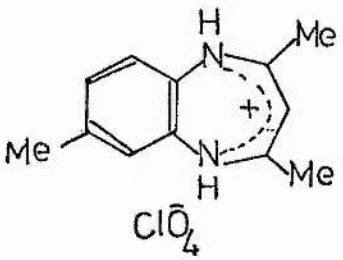


(111)

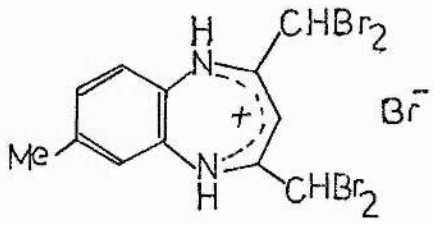
These results are thus compatible with the recent report[179] in that the bromine first attacks the 2,4-substituted methyl groups and not the 6,7,8- and 9-positions of the benzene ring of the molecule as was reported earlier. Compound (108) apparently gave only the pentabromo bromide derivative when it was treated with eight equivalents of bromine, but this result is based on the tentative evidence of a mass spectrum alone. It is not possible, however, to show the position of the fifth bromine atom in the

molecule by its fragmentation pattern. The ^{1}H n.m.r. spectrum was also found to be of no assistance in this case.

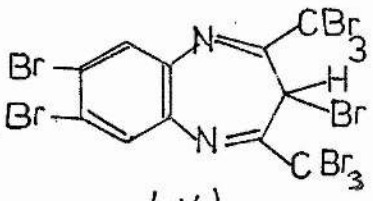
The reaction of compound (112) with eight equivalents of bromine, on the other hand, gave the tetrabromo product (113) (evidence from its n.m.r. spectrum, see Table 4). Hence, it is inferred that the preferred site of attack by a fifth bromine atom on a benzodiazepine must be position 7 of the benzene ring and not position 3 of the seven-membered ring.



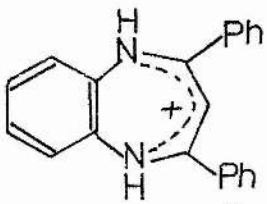
(112)



(113)



(114)



(115)

Williams and co-workers claimed to have isolated compound (114) when a large excess of bromine was added to the compound (108). In view of this, it is reasonable to expect a tribromomethyl or a 7(8) bromo derivative of compound (112) on treatment of it with eight equivalents of bromine. These results tend to suggest that a very high concentration of bromine with respect to the

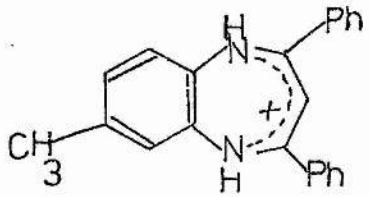
benzodiazepine is essential in order to attack the 7- and 8-positions of the molecule and also that bromine will not replace the hydrogen atoms of the methyl group substituted in the 7-position. The quantitative amount of bromine required to bring about attack at these sites still remains to be investigated.

When six equivalents of bromine were added to the phenyl substituted benzodiazepinium salt (115) only a monobrominated derivative was obtained. However this is again based entirely on the evidence of its mass spectrum. The compound (116) with eight equivalents of bromine gave only a dibromo derivative. In both of these cases, however, it was not possible to ascertain the position of attack by the bromine from the spectrum. However, it is apparent from the mass spectra of these compounds that the phenyl ring is not attacked by the bromine in either case (see later discussion of mass spectrum).

An attempted synthesis of 3-phenyl-1,5-benzodiazepinium perchlorate, in order to study its electrophilic substitution reaction, did not provide the desired product.

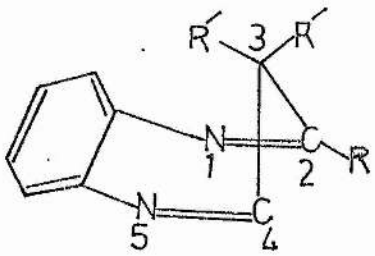
Benzodiazepine molecules are known to take up boat conformations[125,180-181] (117) which are, however, rapidly inverting at room temperature. It has been suggested[181] that any substituents larger than H at the 3-position of the benzodiazepine will cause crowding over the π-electrons system of the benzene ring. An attempted preparation of 2,3,3,4-tetrasubstituted derivative has been shown to give compound (118)[181]. Thus a single 3-substituent will tend to be directed away from the benzene ring to obviate interaction with the π-electrons system.

If this is so, then it may also contribute to the failure to

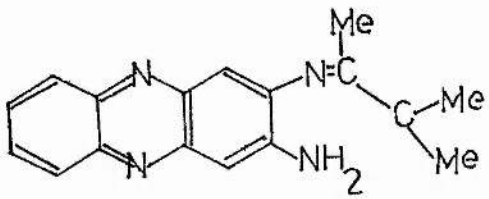


ClO_4^-

(116)



(117)



(118)

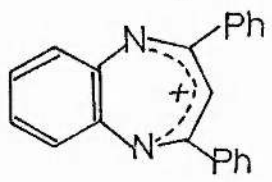
synthesise 3-phenyl substituted benzodiazepine.

Mass Spectra:

Like the dihydrodiazepinium perchlorate salts, the benzodiazepinium perchlorates were also involatile. Hence, these perchlorates had to be converted into their iodides. These are readily available from the perchlorates by metathetic reaction with potassium iodide in methanol.

The benzodiazepinium salts investigated showed low intensity peaks at the m/e value corresponding to the molecular ion of the salt, but this is most likely to be the ^{13}C-isotope peak of the free base[c.f. 182]. Thermal dissociation of the salt, where possible, would therefore appear to precede electron bombardment. For the 2,4-dimethylbenzodiazepinium salt,

the most intense peak in the molecular ion cluster is characteristically that of the base. For 2,4-phenyl-substituted derivatives, however, the (M_{base}-1) peak is of equal intensity to that of the base (i.e. M^+-1). The former is probably due to the loss of the second N-hydrogen atom to give a resonance stabilised cation (e.g. 119), isoelectronic with the Wheland intermediate.



(119)

Whereas the chief fragmentation process in the dihydro-diazepines, confirmed by the presence of metastable peaks, was the elimination of the $N^1—C^2$ fragment, in the benzodiazepines such a breakdown pattern is unlikely because of annellated benzene ring. The high resolution results of the benzodiazepines are shown in Table 3.

Table 3.

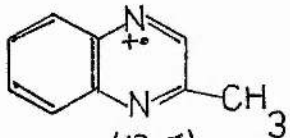
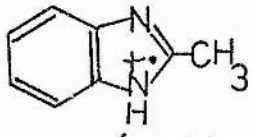
m/e	Structure	Formula	Found	Required
172		$C_{11}H_{12}N_2$	172.1000	172.1000
144	 (42 %)	$C_9H_8N_2$	144.0679	144.0687
132	 (83 %)	$C_8H_8N_2$	132.0681	132.0687

Table 3. (cont)

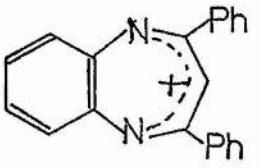
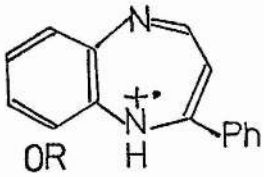
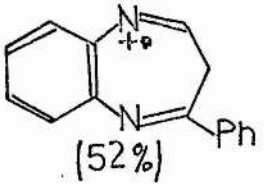
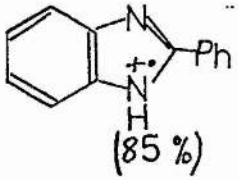
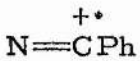
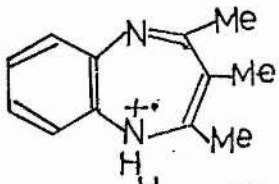
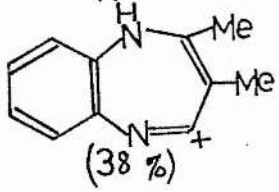
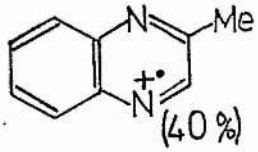
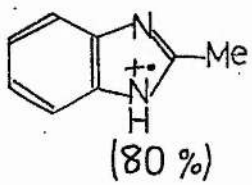
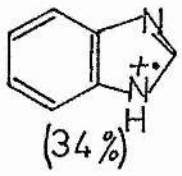
m/e	Structure	Formula	Found	Required
295		$C_{21}H_{15}N_2$	295.1227	295.1235
220	 OR  (52%)	$C_{14}H_{12}N_2$	220.0992	220.1000
194	 (85 %)	$C_{13}H_{10}N_2$	194.0837	194.0843
103		C_7H_5N	103.0534	103.0536
186		$C_{12}H_{14}N_2$	186.1165	186.1157
171	 (38 %)	$C_{11}H_{11}N_2$	171.0925	171.0922
144	 (40 %)	$C_9H_8N_2$	144.0796	144.0687
132	 (80 %)	$C_8H_8N_2$	132.0685	132.0687

Table 3. (cont.)

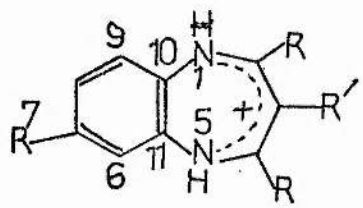
m/e	Structure	Formula	Found	Required
118	 (34%)	$C_7H_6N_2$	118.0646	118.0531

It may thus be seen that the predominant breakdown products are quinoxaline and benzimidazole species.

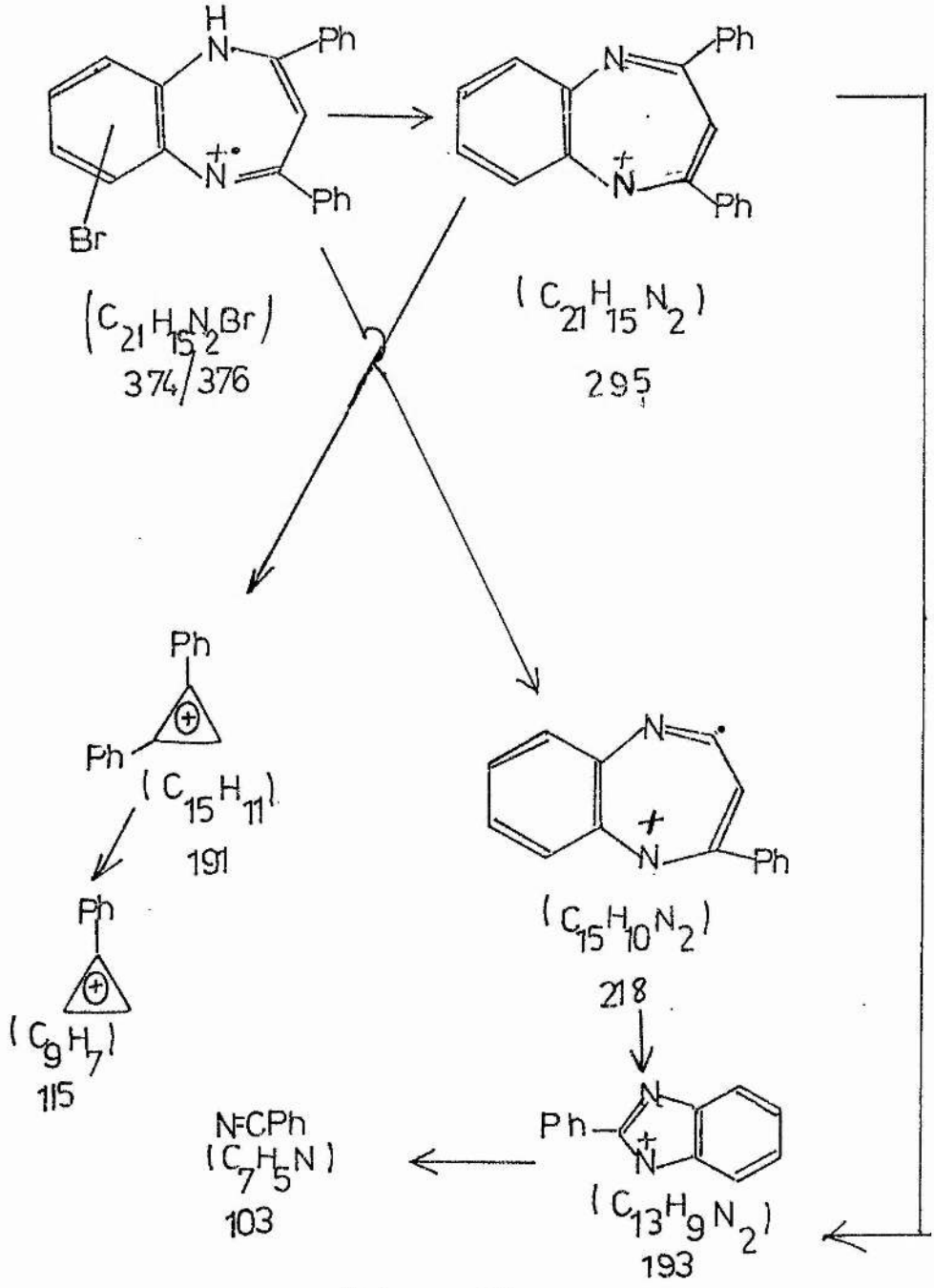
The mass spectrum of the monobrominated 2,4-diphenyl benzodiazepinium salt shows that bromination did not take place in the substituent phenyl group. The following fragmentation patterns may be possible (Scheme 10).

Table 4. ^{1}H N.m.r. Spectra of Benzodiazepinium Salts (120) for DMSO (τ Values)

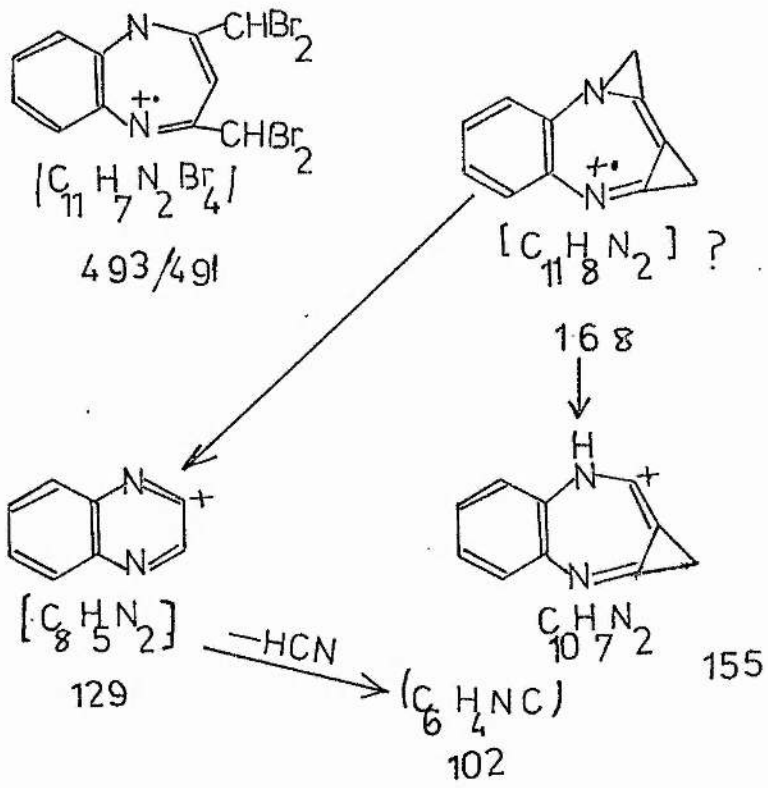
C_3H	Benzo-	R	R^7	NH	R'
5.63(s)	3-3.66(m)	CH_3, 8.1(s)	H	1-1.33(br)	H
5.84(s)	3.24-3.32(1H, d) 3.6-3.67(1H, d) 3.72 (1H)	CH_3, 8.24(s)	CH_3, 7.96(s)	0.2-0.4(1H,br) 0.4-0.6(1H,br)	H
5.02(s)	2.8-3.2(m)	Ph, 2.12-2.6(m)	H	-0.3-(-0.5), br	H
5.1(s)	3.0-3.34(m)	Ph, 2.16-2.6(m)	CH_3, 7.86(s)	—	H



(120)


H
N
Ph
Ph
Br
(C21H15N2Br)
374/376
(C21H15N2)
295
Ph
Ph
(C15H11)
191
Ph
(C9H7)
115
N
Ph
(C15H10N2)
218
N=CPh
(C7H5N)
103
Ph
(C13H9N2)
193

Scheme 10



Scheme 11

Table 4. ^{1}H N.m.r. Spectra of Brominated Benzodiazepinium Salts

Compound	Solvent	C_3H	Benzo	$CHBr_2$	CH_2Br
110	DMSO	2.56(s)	1.32(m)	2.36(s)	7.38(s)
111	DMSO	3.68(s)	2.73(m)	2.4(s)	—
111	conc. H_2SO_4	CH_2,7.1(m) (2H)	3.5-3.6(m)	2.23-2.4 (m)	—
113	DMSO	3.7(1H,s) Me,7.54(s)	2.2-2.36(1H,d) 2.52-2.54(1H,d) 2.72(1H,s)	2.74(2H,s)	—

In conclusion, it is apparent that the behaviour of benzodiazepines towards electrophiles differs markedly from

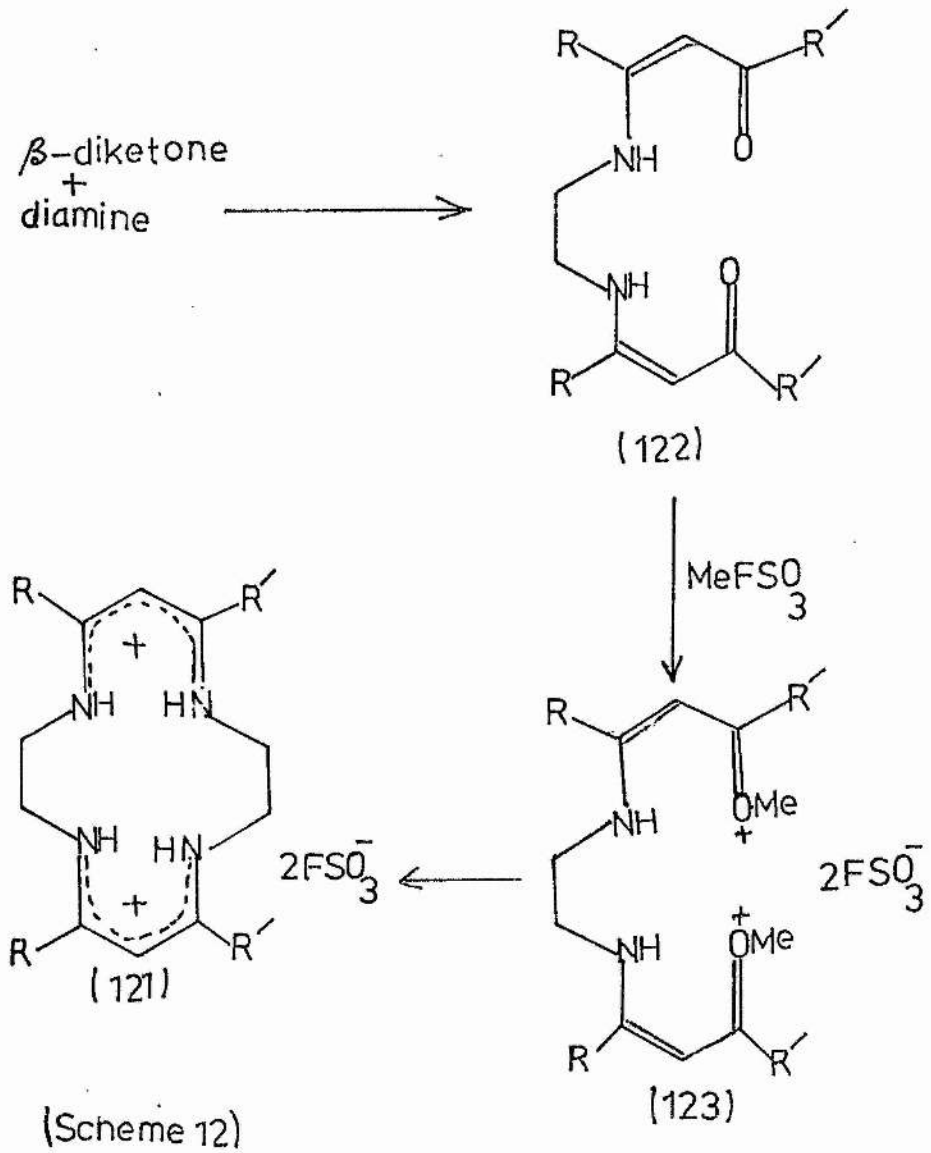
that of dihydrodiazepines. Benzodiazepines are generally less stable than dihydrodiazepines and this lower stability is partly due to the complicated interactions between the π-electrons systemsof the two rings.

DISCUSSION

Part III

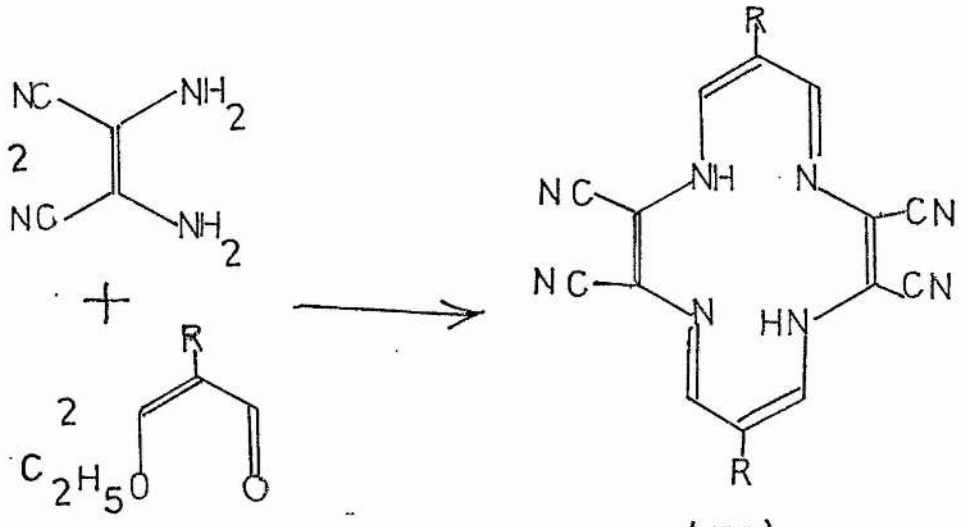
Macrocycles

Simpler macrocycles[165, 166], for example (121) have been prepared as intermediates in the preparation of possible model compounds for corrins and porphyrins. One possible route for their synthesis is the reaction of β-diketones with the diamines under neutral conditions (see introduction section)[120]. The bisoxoenamine (122) thus formed can be methylated to give the salt (123) which reacts with the diamine to give the cyclised product (121), as shown in Scheme 12.



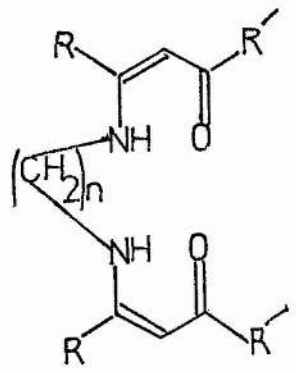
(Scheme 12)

Recently[183], the compound (124) has been prepared by the reaction of 2-alkyl-3-ethoxyacroleins with diaminomaleonitrile.



(124)

In the present work, the following simpler macrocycles were prepared from the diketones and the appropriate diamines according to Scheme 12.



(Bisoxoenamine)

(125)

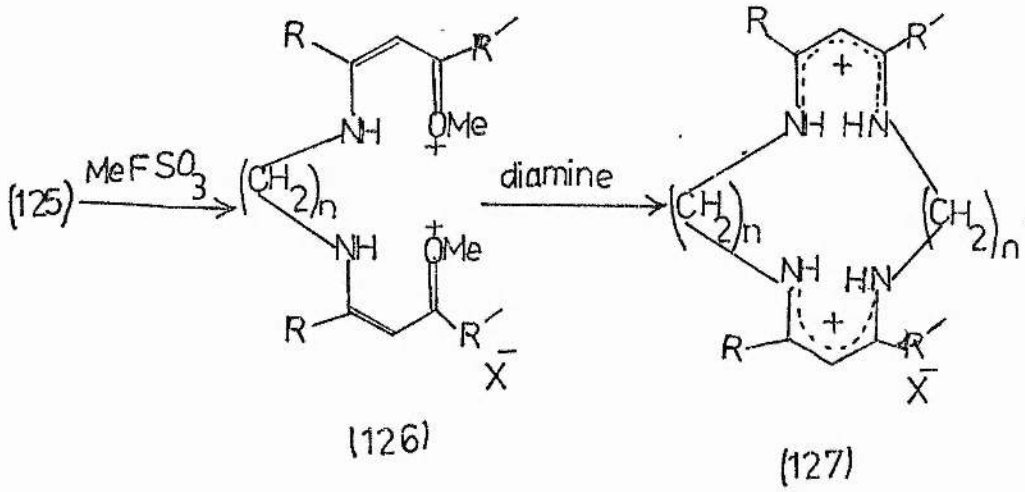
a, R=R'=Me, n=2

b, R=Me, R'=Ph, n=2

c, R=Me, R'=Ph, n=3

d, R=R'=Me, n=3

e, R=R'=Me, n=cyclohexane

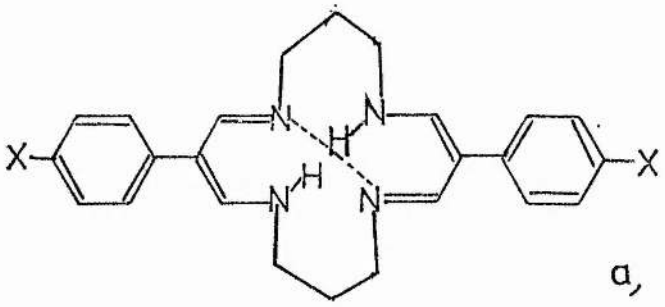


(126) a, R=R'=Me, n=2, was isolated. The rest of the methylated analogues of 125b-125e were used without isolation.

(127) a, R=R'=Me, n=2, and b, R=Me, R'=Ph, n=2 were isolated as solids. The cyclised analogues of the methylated products of (127c-e) could not be obtained in solid forms (see experimental section).

A variety of 7-membered ring compounds were prepared from vinamidinium salts by an 'ammonia method' (see section on preparation of dihydrodiazpines). An attempted cyclisation of an open-chain 1,5-pentadienium salt by this method but using 1,3-diaminopropane to give an 8-membered ring compound, however, gave instead a 16-membered macrocycle (128a). Diazocines seem to be difficult to obtain, for although 1,3-butadiyne forms a 7-membered ring compound with ethylenediamine[121], similar attempts to prepare the 8-membered ring analogue have led to the formation of a mixture of 6-membered derivatives[184]. Likewise, whereas β-diketones form dihydrodiazpines with

ethylenediamines, they have been reported to give a mixture of 6-membered ring analogues with 1, 3-diaminopropane.



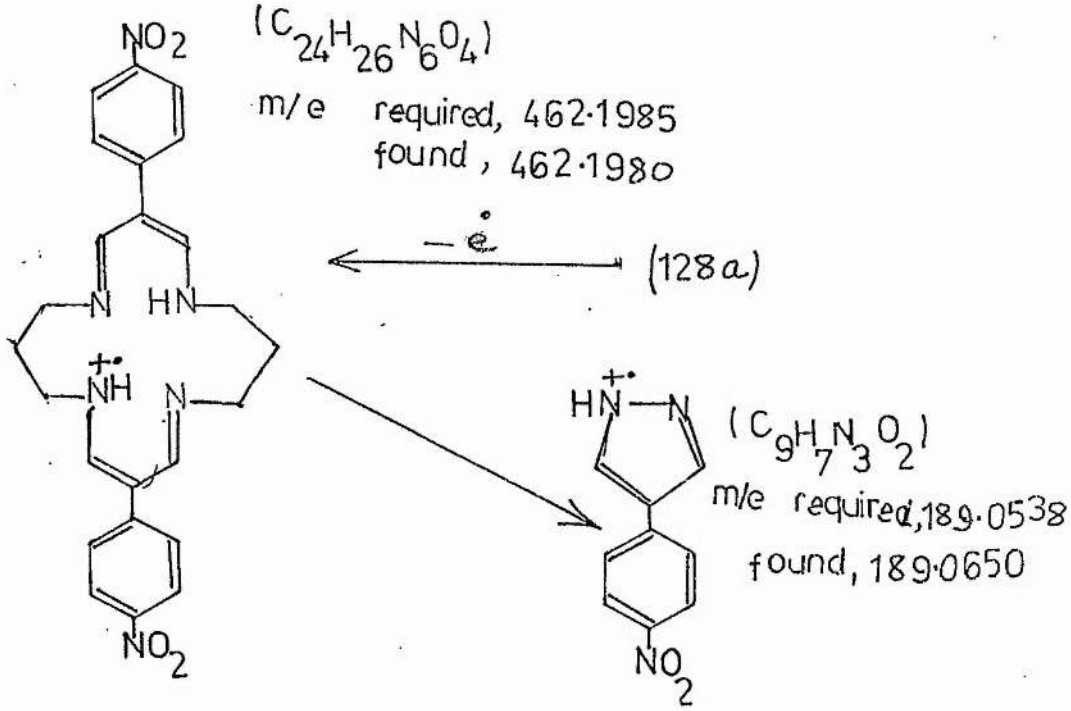
a, X = NO_2

(128)

Attempts to isolate the macrocycle (128), (X=H, or Br or Cl or Me) from their corresponding open-chain vinamidinium salts were unsuccessful. The compound (128a) is intense purple-black. This could be ascribed to the vinamidine and the nitro portions interacting intermolecularly as donor-acceptor molecules to form the charged complexes. Since the base (128a) is formed from the salt of the corresponding open-chain compound, it is likely that the nitro substituent may be playing an important role as a strong electron-withdrawing group to render the molecule less basic. The nitro group may also contribute to the low solubility of compound (128a). Because of its low solubility in a number of solvents, it was not possible to record its ^{1}H n.m.r. spectrum.

The compound (128a) was characterised from its mass spectrum.

In view of the interesting properties shown by dihydrodiazepinium salts, it is of interest to speculate on the importance



of the well-defined geometry of the seven-membered ring in these reactions. Thus, the 1, 5-diazapentadienium system, held in a planar configuration, represents the reactive part of the molecule and so the groups preserving this geometry should be chemically irrelevant unless the pentadienium system is distorted by such groups. This may be the case for the tetrahydrodiazocinium ion, which still remains to be synthesised.

Simpler macrocyles, e.g. (121), potentially contain the vinamidinium system, and the meso position is thought to be chemically equivalent to the 6-position of the dihydrodiazepines.

However, this compound does not undergo electrophilic attack with the molecular bromine. It is possible, therefore, that the vinamidinium system may be distorted within the 14-membered ring compounds, and thus its properties may be modified.

DISCUSSION

Part IV

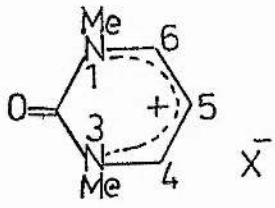
2-Oxo- and 2-Thioxo-5-Aryl-Dihydropyrimidinium Salts

Introduction

It is apparent from the preceding sections that the chemistry of the vinamidinium system is influenced by both steric factors and by the geometrical environment of the system. It is of interest, therefore to alter the electronic nature of the substituents adjacent to the vinamidinium system (c.f. benzodiazepine section) and investigate the changes in properties. To accomplish this end, an attempt was made in the present work to cyclise glycinamide with phenylmalondialdehyde to produce 2,3-dihydro-2-oxo-6-phenyl-1,4-diazepinium salt, but no such product was isolated[c.f. 119]. Recently, one such diazepine has been synthesised, but its properties were not studied. However, 2-oxo- and 2-thioxo-1,2-dihydropyrimidinium salts are made readily by the condensation of a urea or thiourea with a β-dicarbonyl compound, and their properties have been investigated recently[47].

The studies of these compounds have revealed that like the dihydrodiazepinium salts, the dihydropyrimidones undergo bromination and deuteriation at the 5-position, which is equivalent to the 6-position in dihydrodiazepines. However, the electrophilic attack is considerably slower, and no deuteriation of the dihydropyrimidones occurs at room temperature. Investigations of the kinetics and mechanisms of deuteriation[185,186] and bromination[187,188] of the 1,3-dimethyl-2-oxo-dihydropyrimidinium ion (129) had suggested that these reactions do not proceed by simple electrophilic substitution but rather by a stepwise process involving the initial formation of a covalent hydroxy (or deuterioxy)-adduct (130), which then, as an enamine, undergoes electrophilic attack at the 5-position.

The adduct (130) has been observed spectroscopically. This electrophilic behaviour thus differs markedly from the electrophilic substitution of dihydrodiazepines and of benzene derivatives.



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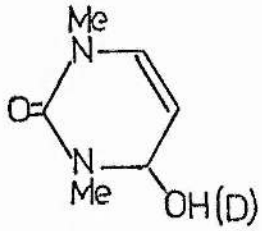
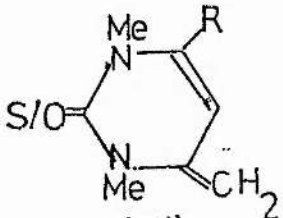


(130)



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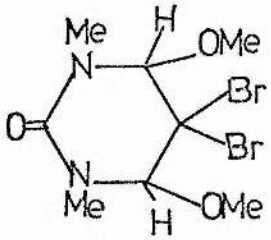
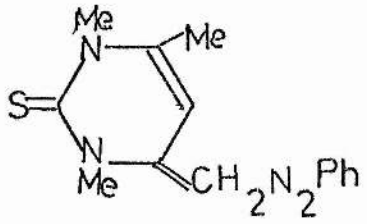


(132)

In contrast with the dihydrodiazepines bromination and deuteriation can also take place at the methyl groups of the 4 and 4,6-dimethyl analogues of dihydropyrimidones. The mechanism probably involves the exocyclic methylene bases (131). Similarly attack by bromine at the 2,4-methyl substituents in the benzodiazepines has already been noted. In the present case, the dibromo derivative (132) has also been isolated, and evidence for the intermediacy of a covalent hydrate has been pointed out recently[189].

The oxodihydropyrimidinium salts differ from dihydrodiazepinium salts in being inert to N-chlorosuccinimide and to nitrating acids. In addition, 4-methyl and 4,6-dimethyl-oxo- and thioxo-derivatives have been shown to couple at the methyl

groups with diaz onium salts to give, e.g., the compound (133)



(133)

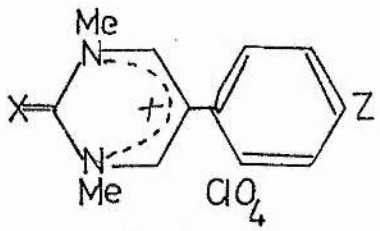
This diazo coupling is presumed to involve attack at the exocyclic methylene bases (131) which may be present in equilibrium with the salts. 5-Halogeno-oxo-(or thioxo)-dihydropyrimidinium salts do not undergo nucleophilic substitution of the halogen atoms.

Hence, the ready formation of such bases (131), formation of adducts like (130), and diminished reactivity of 2-oxo- or thioxo-dihydropyrimidinium salts towards electrophiles are in contrast with the behaviour of dihydrodiazepines. These properties demonstrate the salient feature of the conjugated systems present in the oxodihydropyrimidinium nucleus, namely that in this nucleus two stable delocalised systems, the 1,5-diazapentadienium system and a urea-type system, are in competition for the excess of electrons.

5-Aryl-2-oxo- or thioxo- Dihydropyrimidinium Salts

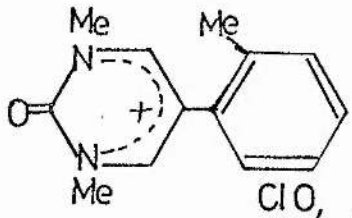
Preparation: In view of the differences in properties of such a perturbed vinamidinium system in the 2-oxo-dihydropyrimidinium salts and the already observed similarities between the dihydro-diazepinium system and their 6-aryl derivatives, it was interesting to compare the behaviour of the 5-aryl-2-oxo-dihydropyrimidinium system with that of unsubstituted analogues. Thus, the 5-aryl substituted derivatives of (134) and (135) were synthesised from the corresponding arylmalondialdehyde and the N,N'- dimethyl urea or thiourea. Since N-unsubstituted derivatives can exist in prototropic

equilibrium with hydroxy- or mercapto-pyrimidine forms, it was imperative to lock the compounds as oxo- or thioxo-derivatives by using an N,N'-disubstituted urea.

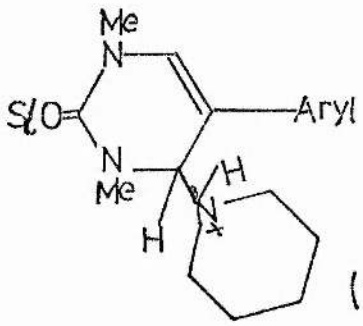


(134)

a, X=O, Z=H
b, X=S, Z=H
c, X=O, Z=OMe
d, X=S, Z=OMe
e, X=O, Z=NO_2
f, X=O, Z=Br



(135)



(136)

It is worth noticing that whereas the 3-aryl vinamidinium salts were readily cyclised with N,N'-dimethylethylenediamine to form the 7-membered ring compounds, the corresponding vinamidinium salts in the present case did not react with N,N'-dimethylurea, presumably because the latter is a much weaker nucleophile than the diamine. In contrast with the ready formation of the compounds (134a-f) at room temperature, preparation of the derivative (135) required heating under reflux for ca 4 hrs in n-butanol (c.f. section on preparation of dihydrodiazepines).

Behaviour towards Electrophiles

In attempted brominations of the 2-oxo- and 2-thioxo-5-phenyldihydropyrimidinium salts in a variety of solvents no reaction took place. This behaviour thus differs from that of their 6-aryldihydrodiazepinium counterparts and from their 5-unsubstituted

6-membered ring analogues. In view of the reduced reactivity of the vinamidinium system due to the 2-oxo- or thioxo- groups, as reported in the case of 5-unsubstituted dihydropyrimidones, and the diminished rate of bromination of the 6-phenyldihydrodiazepinium cation compared with the unsubstituted analogue, it is reasonable that this reactivity would be lowered even further in the case of 5-aryl-2-oxo- or thioxodihydropyrimidinium salts.

The phenyl ring can only interact conjugatively by electron withdrawal from the vinamidinium system, which is in competition with the urea type system, and there will consequently be reduced electron density at the p-carbon of the phenyl ring (see section on properties of dihydrodiazepines). Similarly there was no reaction of bromine with the compound (134c). These compounds also remained unattacked by N-bromosuccinimides.

Reactions with Nucleophiles

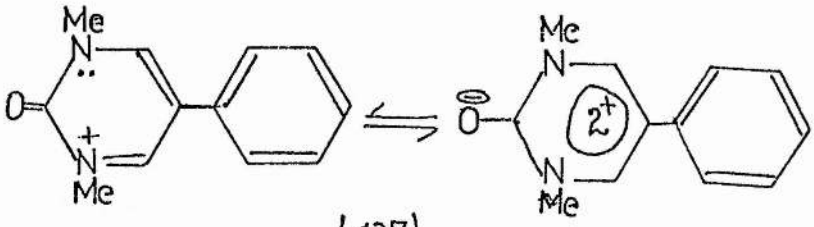
The 5-aryldihydropyrimidones, like their unsubstituted analogues, but unlike the dihydrodiazepinium cations, formed adducts of the type (136) with piperidine. Their formation was observed spectroscopically, by a shift of the absorption maximum to a shorter wavelength in the u.v. spectrum in each case. The ^{1}H n.m.r. showed upfield shifts of the 5-proton by τ ca 3 and that of 6-proton to τ ca 4, thus demonstrating the loss of the conjugated system of the 6-membered vinamidinium system. These signals were consistently at lower field for the thioxo-compound than for their oxo-analogues. These adducts may be compared with the stable Meisenheimer complexes obtained from nitroarenes. The similarity of the chemical shifts of the protons

at C-4 and C-6 in both the N-methyl piperidine and pip eridine adducts indicate that the latter are N-protonated.

In view of the 'transdiazepination' reactions referred to in an earlier section, it was surprising to find that there was no such reaction of the compound (134a) even with a ten fold excess of N, N'-dimethylethylenediamine especially since urea is a better leaving group than ethylenediamine, which is also a better nucleophile than urea.

N.m.r. Studies

The ^{1}H n.m.r. spectra of the oxo- and thioxo-dihydropyrimidinium salts resemble those of other 1,5-diazapentadienium cations in that the signals for 4- and 6-protons appear at much lowerfield than those for 5-protons in the case of 5-unsubstituted products. However, in the present 5-aryl substituted analogues the signals for 4- and 6-protons appear at significantly lower field than in the case of corresponding dihydrodiazepinium salts. This again reflects the competition by the oxo- and thioxo- groups for the electrons of the vinamidinium system, and includes the effects of inductive deshielding together with mesomeric deshielding due to canonical form (137). The signals for the protons in the thioxo compounds appear at lower field than those of the oxo-analogues, indicating that the major deshielding mechanism is conjugative. The 4- and 6-protons are further deshielded by the 5-aryl substituents in each case compared with the unsubstituted cations.



(137)

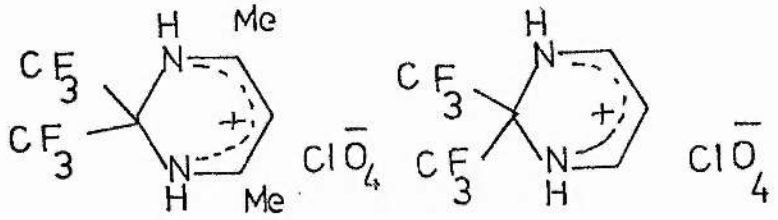
Similarly, the ^{13}C n.m.r. signals for the 1,5-diaza-pentadienium carbon atoms in the 2-oxo- or 2-thioxopyrimidinium salts uniformally appear at lower field than in the case of dihydrodiazepinium salts. A similar trend is shown by the p-carbon of the 5-phenyl substituent (see ^{13}C n.m.r. section).

Electronic Spectra

The oxo- and thioxo-pyrimidinium salts generally show two maxima in their u.v. spectra. Those at longer wavelength are characteristic of the 1,5-pentadienium system, and the shorter wavelength absorptions are associated with the phenyl and urea chromophores. The latter are more intense for the thioxo- than for the oxo-compounds, in keeping with the known higher absorption of thiourea itself in comparison with urea, and with the greater polarity of the thioxo group. 5-Aryl groups cause a bathochromic shift and decreased extinction coefficients in the case of the oxo-compounds (as in dihydrodiazepinium salts), but a hypsochromic shift and increased exctinction coefficients in the case of the thioxo derivatives.

Fluorescence Spectra

It is very intriguing that the 5-phenyldihydropyrimidinium and the 5-o-tolyl-dihydropyrimidinium salts showed a specialised-electronic absorption-emission spectra. Both these compounds showed violet fluorescence in water, methanol, ethanol, ether, and acetonitrile. Recently, the compounds (138) and (139) have been reported to display this special property of being fluorescent[190].



(138) (139)

It is of interest that the incorporation of electron-withdrawing substituents such as fluoro and oxo at the 2-position of the vinamidinium system results in the electronic spectral properties of these compounds being markedly altered. In the case of the 5-aryl-2-oxo- or thioxodihydropyrimidinium compounds (134a) and (135) it is suggested that the extended conjugation provided by the phenyl ring may be responsible for such behaviour. Similar spectral studies of the compounds (134c and 134e) show these compounds to be non-fluorescent. This can be ascribed to interference with the conjugative interaction between the phenyl group, the vinamidinium system and urea type system by the strong electron-withdrawing effect of the nitro group; a similar effect may be produced inductively by the methoxy group.

The o-tolyl-2-oxo-dihydropyrimidinium compound (135) was only faintly fluorescent in acetonitrile. The situation is thus intermediate between that for the nitro compound and that for its unsubstituted analogue. Disruption of the coplanarity between the two rings by the adjacent methyl substituent, and hence of the conjugation, presumably accounts for the reduced intensity of fluorescence in this case. The 5-phenyl-2-oxo-dihydropyrimidinium cation showed a fluorescent maximum at ca 463 nm in acetonitrile and a symmetrical spectrum. The excitation spectrum, however, showed two absorption maxima at 335 and 390 nm which was rather similar to the absorption spectrum of the 2-oxo-dihydropyrimidinium salt. The fluorescent lifetime for this compound was calculated to be ca 28.8 ns.

A parallel between the electronic spectra of dihydro-diazepines and vinamidines and those of the cyanines has been remarked upon earlier. It is interesting that since many laser dyes are cyanines or merocyanine dyes which have rigid structures (like the vinamidinium system), further studies of such compounds (134a) with relatively short conjugated system might prove interesting as possible laser dyes in the ultraviolet region.

It is thus apparent from comparative studies of compounds containing undisturbed vinamidinium systems with compounds wherein a vinamidinium system is disturbed electronically, as in dihydropyrimidinium salts, or sterically, that the properties of the system,for example in its behaviour towards electrophiles and nucleophiles, are significantly modified by this distortion.

DISCUSSION

Part V

Carbon-13 Nuclear Magnetic Resonance Spectra

Introduction

The potential use of ^{13}C n.m.r. spectroscopy as a standard tool in organic chemistry has recently gained realisation because the major problem of sensitivity can now be overcome in the Fourier Transfer mode of operation. In a standard spectrum the noise decoupling of the proton resonances enables the chemical shift (σ) to be measured with accuracy in ppm. from the reference TMS. Although the factors determining the chemical shift are only incompletely understood[191] at present, it seems, among other things, to relate to the charge density at the carbon atom[192,193]. ^{13}C n.m.r. studies of molecules which have complete cyclic conjugated systems clearly show that the chemical shifts are little affected by the presence of ring currents, but are more sensitive to stereochemical factors[194]. Since the properties of 2,3-dihydrodiazepinium salts are closely connected with the charge distribution in the molecule, they are well suited for ^{13}C n.m.r. studies.

In the present work, the ^{13}C n.m.r. chemical shifts of the open-chain 1,5-diazapenta.dienium salts, dihydrodiazepinium salts, dihydropyrimidinium salts, and 1,5-benzodiazepinium salts are assigned and briefly compared.

The proton n.m.r. spectra of the 6-unsubstituted dihydrodiazepinium salts had previously indicated[9] the alternating polarity of the conjugated part of the ring in that signals for the 5-7-protons appear at much lower field than signals for the 6-protons. These results are confirmed by the ^{13}C n.m.r. studies which show that there is an enormous difference in chemical shift between the

C-6 (meso-carbon, σ ca 90 p.p.m.) and the C-5,7 (α-carbons, σ ca 160 p.p.m.). These results are in accord with studies on cyanines, which have a related electronic system, and with MO-LCAO calculations on α, ω-diazapolymethines. Similar results have been reported for the isoelectronic pentadienide anion[195]. Recently[97], it has been shown that the C-2 in 1,2-diaminocyclopropenium system resonates at ca 99 p.p.m. Such results, thus, confirm the electron-rich character of the vinamidinium system. The signal for the meso-carbon of the vinamidinium system resonates at much higher field than normally found for nitrogen heterocycles[196] but approaches that of the meso position in porphyrins[197], and that of the methine carbon in the enol-form of β-diketones[198].

Effects of Substituents on Vinamidinium System

It has been pointed out that conjugative interaction of the dihydrodiazepinium system with the phenyl substituents at the 1,4,6-positions is necessarily electron-donating and electron-withdrawing at the 5,7-positions[9,12]. Again, the ^{13}C n.m.r. studies of these compounds demonstrate the fact very well.

The 6-phenyl substituent causes a downfield shift of the meso-carbon signal by ca 14.6 p.p.m. relative to its unsubstituted analogues (σ 88 p.p.m.). (See Table 5). This effect is qualitatively much the same as that observed on another benzene ring e.g. in biphenyl. The substituent effects seem to be additive, e.g., with the introduction of N-phenyl substituent (σ 105.5 p.p.m.) and N,N'-diphenyl group (σ 107.6 p.p.m.) a further downfield shift of ca 2.5 ppm. is observed for each of the two N-phenyl groups relative to the 6-phenyl compound (140a, Table 5).

Chemical Shifts of Phenyl Peaks

Mode of Assignment: One main advantage of the absence of coupling in standard ^{13}C n.m.r. spectra is that peaks may often be readily assigned to each position in aryl groups. In the assignment of the phenyl signals it has been assumed that the most downfield peak is due to the 1-carbon atom, and that the p-carbon atom gives rise to the other peak of low intensity. In general, the o-carbon peak was adjacent to that of the p-carbon, but in cases of doubt, the signal at 129.5 $\pm$ 1 p.p.m. was considered to be due to the m-carbon. The carbon atoms in benzene itself resonate at 128.5 p.p.m. downfield of TMS and the m-carbon atoms in its derivatives would be expected to show the least deviation from that norm.

However, when more than one phenyl group was present in a molecule, for example, in the 1,4,6-triphenyl dihydrodiazepinium salt (140 g, Table 5), the peaks were assigned as shown in the following example.

Experimental Results		Relative Peak Heights
123.17	A	4
126.99	B	1
128.5	C	6
129.7	D	4
138.66	E	1
145.43	F	2

These values may be compared with values obtained for 6-phenyl- and 1,4-diphenyl-dihydrodiazepinium cations.

6-Phenyl has	6(1)	138.71	i.e., c.f. E
	6p	126.17	i.e., c.f. B
	1,4-o	122.62	i.e., c.f. A

1,4-Diphenyl- has 1,4(1) 144.97 i.e., c.f. F

These correspond reasonably to signals E, B, A, F of the 1,4,6-triphenyl derivative; so it is assumed that these latter signals refer to corresponding atoms in this molecule.

B [6(p)] in the triphenyl compound is shifted by +0.8, A and F by ca 0.5. If similar shifts are applied to other observed signals in the 6-phenyl- and 1,4-phenyl compounds other than to the m-peaks then we get,

$$1,4\text{-}p = 128.29 + 0.5 \approx 128.8$$

$$6\text{-} = 127.19 + 0.8 \approx 128$$

$$1,4\text{-}m = 129.73$$

$$6\text{-}m = 128.66$$

This would assign D(129.7) to the 1,4-m atoms. C probably includes 1,4-p, 6-o, and 6-m. This also fits the peak heights. These results were checked with the higher resolution spectrum (Scan 10,000) obtained from a sample mixed with $Cr(acec)_3$.

For the assignment of the 1,4-p-anisyl-6-phenyl compound (140 ℓ, Table 5) it was assumed that signals for the 6-phenyl group carbon atoms are not shifted or very slightly shifted downfield, and the usual empirical values for the methoxy group increments were taken into account.

Predicted approximate shifts		Experimental results
1,4-m	117	116.56
1,4-o	124.5-126	125.82
6-p	127-128.5	128.28
6-o	128-128.5	129.58
6-m	128.5-129	129.83
1,4(1)	138	139.98
6(1)	138.5-139	140.34
1,4-p	159.5-160	160.93

Thus, these empirical results fit the experimental values.

These results were cross-checked with the spectra of 1,4-p-dianisyl- and 1,6-diphenyl-dihydrodiazepinium salts (See Table 5).

Chemical Shift of the p-Carbon Atom

The electronic interaction between substituent phenyl groups and the vinamidinium system can be observed from the chemical shifts of the p-carbon atoms of the phenyl ring. The electron-withdrawing ability of 1,4,6-phenyl groups of the vinamidinium salts is apparent from the upfield shift of their p-carbon resonance (140g, Table 5), while the opposite effect is shown by the corresponding signal of the 5(7)-phenyl groups (Table 11).

Since the chemical shift of the m-carbon atom is virtually independent of electronic effects, the quantity σ(m)- σ(p) should give an indication of the efficiency of the conjugation (Table 22). It is also apparent that the efficiency of the conjugation in di- (140f, Table 22) and tri-phenyl substituted derivatives (140g, Table 22) is diminished due to increased electron delocalisation, and the difference (σm- σp) is reduced compared with the 6-phenyl analogue (140a, Table 22).

Steric effects

The lessened conjugation of a 6-phenyl group with the dihydrodiazepinium ring when it is flanked by a 5-methyl substituent (140j and 140k, Table 22) is also evident. This is presumably because the phenyl ring is forced out of coplanarity with the seven-membered ring. The methyl substituent at C(2) shifts the meso-carbon atom signal downfield.

Variable Temperature N.m.r. Studies

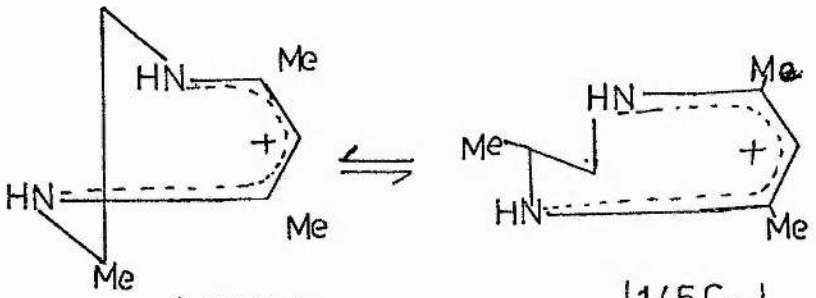
The studies of variable temperature ^{1}H n.m.r. had shown earlier[9] that the dihydrodiazepine ring has a half-chair shape which inverts rapidly at ambient temperature. These results were confirmed by similar studies of ^{13}C n.m.r. on the compounds (145a-d), which were prepared by the literature methods. The results are shown in Table 14.

At $+40^{\circ}$, the methyl signals for the 2,2,5,7-tetramethyl-dihydrodiazepine (145a, X=Cl) appear at 25.28, 25.48 and 27.24. When the solution is cooled to -40° there are four signals, at 23.44, 25.63, 26.57 and 27.26. The peaks at ca 25.5 and ca 27.25 persist throughout the temperature range but the peak at 25.28 ($+40^{\circ}$) disappears below zero to be replaced by two signals at still lower temperatures. The persistent signals may be ascribed to the 5,7-methyl groups, while the other signals arise from the 2-methyl groups, which appear as distinct quasi-axial and quasi-equatorial groups at low temperatures, but are averaged out by inversion at higher temperatures.

In the case of (145b, X=H), however, there are only two signals (at 23.17 and 24.84) at $+40^{\circ}$ and only three (at 23.13, 24.71

and 26.51) at -40°. At +40° the signal at ca 23.15 is much greater than that at ca 24.8, but at -40° the ratio is reversed, while at +20°, the two signals are of approximately equal height and are superimposed upon a flat signal. It seems therefore that these two signals arise from the 5,7-methyl groups, and that at +40° an average signal for the two 2-methyl groups is superimposed upon the higher field signal; this superimposed signal disappears when the solution is cooled to ca +20° and then reappears at lower temperatures as two signals due to separate quasi-axial and quasi-equatorial methyl groups, and one of these separate signals is now superimposed on the lower field signal due to the 5,7-methyl group.

The situation is more complex in the case of 2,5,7-trimethyl dihydrodiazepinium salt (145c) because an inversion is not between two equivalent conformers but between two distinct species ($145c_a$) and ($145c_b$).



($145C_a$) ($145C_b$)

Thus when inversion is rapid, there should be one signal due to the 2-methyl group, and two due to each of the 5,7-methyl groups, 5,7-ring atoms, and 2,3-ring atoms, while at lower temperatures there should be two signals due to the 2-methyl group, and four signals for each of the 2,3-ring atoms, 5,7-ring atoms, and 5,7-methyl groups. The experimental results

confirm this (see Table 14).

The low temperature spectra of this compound (145c) indicate an approximately equal contribution for the quasi-axial ($145c_a$) and quasi-equatorial ($145c_b$) conformers. This is also in agreement with the earlier findings[9] from ^1H n.m.r. At -50° the two signals due to the protons of the 2-methyl group appear of equal intensity. Hence, in contrast to the behaviour of cyclohexane derivatives, there is no preference for a substituent methyl group in the saturated part of a dihydrodiazepinium ring to adopt an equatorial position. The difference arises from the absence of other axial substituents in the other part of the ring, which in turn leads to an absence of 1,3-diaxial interactions.

The cyclohexanodihydrodiazepinium salt (145d) must be rigid, and cannot invert. In accord with this, its ^{13}C n.m.r. spectrum does not change over the temperature range +40° to -40° (See Table 14).

In assigning the 5,7-methyl signals it has been assumed that for the 2-substituted dihydrodiazepinium salts the chemical shift due to the 5-methyl group is more likely than the signal due to the 7-methyl group to resemble the shift for 5,7-methyl groups in the 2-unsubstituted analogue, since the 5-methyl group is further away from the 2-substituent.

2-Oxo- and 2-Thioxo-1,2-Dihydropyrimidinium Salts

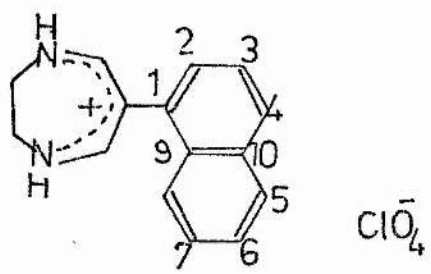
The signals of the meso-carbon atom, of the carbon atoms α- to nitrogens, and of the 2-carbon atom in the 2-oxo- and particularly the 2-thiopyrimidinium salts occur at lower field than the corresponding dihydrodiazepinium salts. This can be

ascribed to the competition between the urea-like and the vinamidinium systems, resulting in a lower electron density in the latter system in these compounds. It may also be due to this competition that carbon (2) signal appears at higher field than in ureas (see Tables 15 and 16). The difference between σ(m) - σ(p), which is a measure of electron density at the p-carbon atom, is small compared with 6-phenyl dihydrodiazepinium salts (see Table 22). This emphasises the competition between urea-like system and the conjugative interaction of the vinamidinium system and the phenyl ring.

1,5-Benzodiazepinium Salts

The signals of each carbon atom in the conjugated part of the 1,5-benzodiazepine occur at lower field than in the corresponding dihydrodiazepines and the dihydropyrimidines (148a-d, Table 20). The difference in structure between the benzodiazepine bases and their related salts is reflected in the difference between the chemical shifts of the 2, 3, and 4 carbon atoms in the two forms.

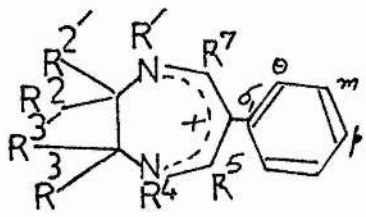
6-α-Naphthyldihydrodiazepinium Salts



^{13}C N.m.r. Spectra of Brominated and Unbrominated 6-α-Naphthyl-dihydrodiazepinium Salt in DMSO [σ, p.p.m. from Me_4Si]

	In Unbrominated	In Brominated
Diazepine $C_{2,3}$	50.02	48.98
Diazepine C_6	101.58	99.36
Naphthalene C_4	125.43	121.58
C_9	134.63	131.58
C_{10}	133.27	134.05
C_1	136.23	136.67
Diazepine $C_{5,7}$	159.74	158.66

The signal at σ125.43 in the unbrominated compound is likely to be C(4) of the naphthalene because of being furthest upfield[c.f. also 173]. If it is accepted that that site to be brominated, then the shift of the signal in the brominated speci es confirms this - its drop in relative intensity because of becoming fully saturated is also observed.



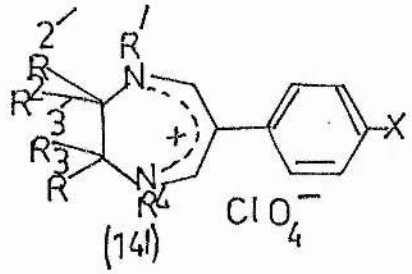
ClO_4^-

(140)

a, R^n=H; h, $R^{2'}$=R^2=$R^{3'}$=R^3=cyclohexano
b, R^1=Me; i, R^1=R^4=CH_2Ph
c, R^2=Me; j, R^5=Me
d, R^1=R^4=Me; k, R^1=R^5=Me
e, $R^{2'}$=R^2=Me; l, R^1=R^4=p-anisyl
f, R^1=Ph; m, R^1=R^4=Et
g, R^1=R^4=Ph;

Table 5. ^{13}C N.m.r. Spectra of 6-Phenyldihydrodiazepinium Salts (140) [σ, p.p.m. from Me_4Si]

Compound	σ(6)	σ(5,7)	σ(2,3)	σ (others)
140a (Acetone)	102.68	157.30	48.70	p, 126.17; o, 127.19; m, 128.66; σ_1, 138.71
140b (Acetone)	104.34	156.93(5) 160.58(7)	48.87(3) 49.27(2)	p, 127.30; , 128.43; m, 129.55 σ_1, 139.83; 1-Me, 57.77
140c (Acetone)	104.83	157.28(5) 159.47(7)	53.75(2) 56.46(3)	p, 127.44; o, 128.27; m, 129.68; σ_1, 139.53; 2-Me, 17.38
140d (DMSO)	102.72	157.95	47.69	p, 126.45; o, 127.90; m, 128.80; σ_1, 139.38; 1,4-Me, 55.28
140e (DMSO)	103.06	158.01(5) 154.03(7)	55.85(2) 59.55(3)	p, 126.42; o, 127.37; m, 128.89; σ_1, 138.71; 2-Me, 24.95
140f (DMSO)	105.5	154.75(7) 159.99(5)	49.17(3) 55.89(2)	1-o, 123.14; 6-p, 126.6; 6o+1-p, 127.86; 6-m, 128.64; 1-m, 129.56; σ_1, 138.65; 1-σ_1, 148.75
140g (DMSO)	107.65	155.28	56.36	1,4-o, 123.17; 6-p, 126.99; 6-o-m+1,4-p, 128.51; 1,4-m, 129.7; σ_1, 138.66; 1,4-σ_1, 145.43
140h (DMSO)	103.48	156.61	61.35	o+p, 127.73; m, 130.06, σ_1, 138.98; 4', 5', 23.54; 3', 6', 31.26 (of cyclohexane)
140i (DMSO)	103.25	157.83	53.63	6-p, 126.48; 6-o, 128.04; 6m+benzyl-o, m, p, 128.62/128.93; 1,4-σ_1, 133.76; σ_1, 138.88; 1,4-methylene, 62.95
140j (Acetone)	105.20	171.81(5) 156.49(7)	49.02(2) 50.32(3)	p, 128.20; m, 12.948; o, 131.86; σ_1, 140.51; 5-Me, 24.36
140k (Acetone)	104.58	169.48(5) 158.24(7)	47.81(2) 48.43(3)	p, 128.05; m, 129.34; o, 132.02; σ_1, 140.76; 1-Me, 57.19; 5-Me, 24.07
1401 (CD_3CN)	109.22	155.81	56.44	1,4-m, 115.86; 1,4-o, 125.82; 6-p, 128.28; 6-o+m, 129.58/129.83; σ_1, 139.98; 1,4-σ_1 140.34; 1,4-p, 160.93; p-OMe, 57.95
140m (DMSO)	102.65	156.94	53.77	p, 126.28; o, 127.78; m, 128.65; σ_1, 139.24



(141)

a, R^n=H, X=Br
b, R^1=Me, X=Br
c, R^2=Me, X=Br
d, R^1=R^4=Me, X=Br
e, $R^{2'}$=R^2=Me, X=Br

f, R^n=H, X=Cl; g, R^n=H, X=I; h, R^n=H, X=NO_2 (NO_3^-)
i, R^1=R^4=Me, X=NO_2 j, R^1=Ph, X=NO_2; k, R^1=R^4=Ph, X=NO_2
l, R^1=R^4=CH_2Ph, X=NO_2; m, R^n=H, X=OMe n, R^2=Me, X=OMe;
o, R^1=R^4=CH_2Ph, X=OMe; p, R^n=H, X=Me; q, R^1=R^4=CH_2Ph, X=Me;
r, R^1=R^4=Et, X=Br

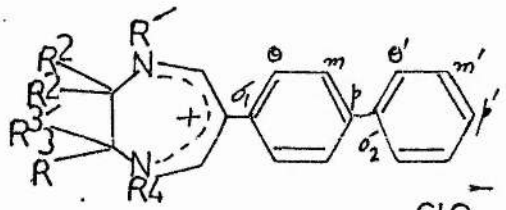
Table 6. ^{13}C N.m.r. Spectra of p-Substituted 6-Phenyldihydrodiazepinium Salts (141)

Compound	σ(6)	σ(5,7)	σ(2,3)	σ(others)
141a (DMSO)	100.74	157.45	47.50	p, 119.31; o, 129.44; m, 131.23; σ_1, 138.23
141b (DMSO)	101.13	155.59(7) 158.78(5)	47.78	p, 119.30; o, 129.35; m, 131.26; σ_1, 138.11; 1-Me, 56.49
141c (DMSO)	101.61	155.36(7) 157.70(5)	52.24(2) 54.55(3)	p, 119.36; o, 129.36; m, 131.36; σ_1, 137.94; 2-Me, 16.84
141d (DMSO)	100.86	157.39	47.44	p, 119.31; o, 129.49; m, 131.21; σ_1, 138.31; 1,4-Me, 55.29
141e (DMSO)	101.74	153.71(7) 157.76(5)	55.64(2) 59.37(3)	p, 119.42; o, 129.27; m, 131.38; σ_1, 137.84; 2-Me, 24.93
141f (DMSO)	101.65	157.31	48.82	o, 128.51; m, 129.98; p. 131.08; σ_1, 137.73
141g (DMSO)	101.71	157.29	48.79	p, 91.76; o, 129.49; m, 137.31; σ_1, 138.48
141h (DMSO)	101.12	157.84	48.93	m, 123.93; o, 127.38; p, 146.11; σ_1, 145.40
141i (DMSO)	100.19	157.85	47.73	m, 123.59; o, 127.54; p, 146.12; σ_1, 145.27; 1,4-Me, 55.28
141j (DMSO)	103.73	155.78(7) 158.12(5)	49.19(3) 59.22(2)	1-o+6-m, 123.43/123.74; 1-p+6-o, 128.48; 1-m, 129.67; 6-p+1-σ_1+σ_1, 145.86
141k (DMSO)	105.76	155.91	56.45	1,4-o, 123.34; 6-m, 123.46; 6-o+1,4-p, 128.68/129.29; 1,4-m, 129.74; 1-σ_1; 145.54; σ_1, 145.73; 6-p, 146.04

cont. overleaf

Table 6. (cont.)

Compound	σ(6)	σ(5,7)	σ(2,3)	σ(others)
141 l (DMSO)	101.51	158.21	53.53	6-m, 123.75; 6-o, 127.84; 1,4-p, 128.29; 1,4 o+m, 128.73/128.97; 1,4-σ_1, 133.51; σ_1, 145.68; 6-p, 146.01; 1,4-methylene, 63.34
141m (DMSO)	102.64	157.26	49.03	m, 114.25; o, 128.86; p, 158.19; σ_1, 131.34; p-OMe, 55.28
141n (DMSO)	102.66	155.38(7) 157.62(5)	52.48(2) 54.80(3)	m, 114.23; o, 128.81; p, 158.19; σ_1, 131.21; p-OMe, 55.26; 2-Me, 16.95
141o (DMSO)	102.1	156.66	52.79	6-m, 113.18; 1,4-o, m, p+6-o, 127.68/128.03/128.59; σ_1, 130.44; 1,4-σ_1, 132.91; 6-p, 157.42; 1,4-methylene, 61.98; p-OMe, 54.35
141p (DMSO)	102.56	157.16	48.80	o, 127.17; m, 129.20; p, 135.37; σ_1, 135.90; p-Me, 20.40
141q	102.21	156.71	52.72	6-o, 127.02; 1,4-o+1,4-m+6-m+1,4-p, 127.66/127.99/128.24; 1,4-σ_1, 132.88; 6-p+σ_1, 134.83/135.90; p-Me, 20.48; 1,4-methylene, 61.98
141r	102.92	157.51	54.61	p, 120.40; o, 130.48; m, 132.04; σ_1, 139.31



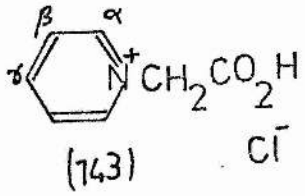
(142) ClO_4^-

a, R^n=H
b, R^1=R^4=Me

Table 7. ^{13}C N.m.r. Spectra of Compounds (142)

Compound	σ(6)	σ(5,7)	σ(2,3)	σ (others)
142a (DMSO)	102.22	157.33	48.81	o, 126.37; p', 127.32; m, o'+m', 126.84/127.69/128.89; p+σ_2, 137.89; σ_1, 139.1
142b (DMSO)	102.64	157.86	48.80	o, 126.42; p', 127.30; m, o'+m', 126.90/127.85/129.0; p+σ^2, 137.91; σ^1, 139.3

Table 8. ^{13}C N.m.r. of Compound (143) in TFA σ (p.p.m.) from TMS

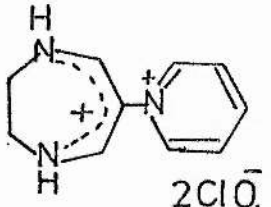


(143)

2	1	β	α	γ
63	170.7	130	147	149

Table 9. ^{13}C N.m.r. of Compound (69) in DMSO σ (p.p.m.) from TMS

σ(6)	σ(5,7)	σ(2,3)	σ_β	σ_γ	σ_α
114.84	149.56	52.27	127.86	144.29	145.58

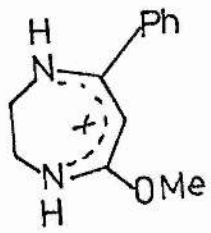


(69)

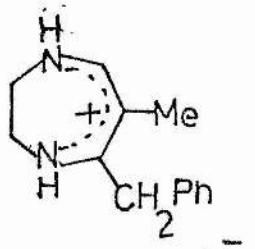
(60)

Table 10.

Compound	σ(6)	σ(5,7)	σ(2,3)	σ (others)
60 (DMSO)	92.14	154.43	56.23	m, 114.73; o, 126.16; 1, 4- σ_1, 138.58; p, 158.98; p-OMe, 55.59



(89)



(77a)

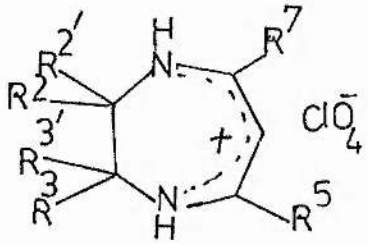
Table 11. ^{13}C N.m.r. Spectrum of Compound (89) in Acetone

σ(p.p.m.) from TMS

σ(6)	σ(5,7)	σ(2,3)	σ(others)
79.05	166.25(7) 170.89(5)	45.64(3) 48.83(2)	o, 128.45; m, 129.84; p, 132.56; 7-σ_1, 137.43; 5-OMe, 58.09

Table 12. ^{13}C N.m.r. Spectrum of Compound (77a) in Acetone

σ(6)	σ(5,7)	σ(2,3)	σ (others)
95.67	158.31(7) 172.76(5)	49.17 50.61	m+(o or m), 128.09; p+(o or m), 129.71; 5-σ_1, 135.52; 5-methylene, 42.39; 6-Me, 19.25

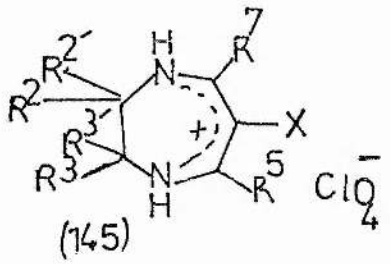


(144)

a, R^5=Me, (picrate anion)
b, $R^{2'}$=R^2=$R^{3'}$=R^3=Me
c, $R^{2'}$=R^2=$R^{3'}$=R^3=R^5=R^7=Me
d, $R^{2'}$=R^2=$R^{3'}$=R^3=R^5=R^7=Et

Table 13. ^{13}C N..m.r. Spectra of Compounds (144)

Compound	σ(6)	σ(5,7)	σ(2,3)	σ (others)
144a (Acetone)	90.59	155.63(7) 167.68(5) (v. small)	49.94(2) 49.02(3)	5-Me, 23.80
144b (Acetone)	90.48	156.24	64.04	Axials/Equatorial-Me, 25.19/21.09
144c (Acetone)	93.26	165.61	62.62	Axials/Equatorials-Me, 25.25/20.82; 5,7-Me, 24.09
144d (DMSO)	90.00	169.88	60.99	Axials/Equatorials-Me, 24.67/20.12; 5,7-Methylene, 30.58; 5,7-Me, 13.78

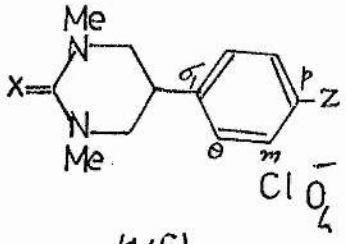


(145)

a, $R^{2'}=R^{2}=R^{5}=R^{7}$=Me, X=Cl
b, $R^{2'}=R^{2}=R^{5}=R^{7}$=Me, X=H
c, $R^{2'}=R^{5}=R^{7}$=Me, X=H
d, $R^{2'}=R^{3'}$=cylohexano, X=H

Table 14. Variable Temperature ^{13}C N.m.r. Spectra of Compounds (145)

Compound	Temp.	σ(6)	σ(5,7)	σ(2,3)	σ(5-Me)	σ(7-Me)	σ(2-Me)
145a (DMSO)	+40°	96.92	164.58(5) 168.76(7)	55.80(2) 60.44(3)	25.48	27.24	25.28
	-20°	96.76	164.33(5) 168.58(7)	55.50(2) 60.28(3)	25.59	27.27	-
	-40°	96.70	164.22(5) 168.51(7)	55.37(2) 60.23(3)	25.63	27.26	23.44 26.57
145b (DMSO)	+40°	92.02	164.97(5) 168.41(7)	55.71(2) 58.89(3)	23.17	24.84	24.84
	+20°	92.02	164.93(5) 168.35(7)	55.61(2) 58.84(3)	23.17	24.80	-
	-40°	91.88	164.69(5) 168.16(7)	55.42(2) 58.74(3)	23.17	24.71	23.13 26.51
145c (DMSO)	+30°	91.97	166.26(5) 168.38(7)	52.17(2) 54.54(3)	23.45	24.33	17.05
	-40°	91.82	166.15(5) 167.90(5) 168.39(7)	53.31(2) 53.76(2) 55.59(3)	23.58 23.72	23.92 24.60	16.15 17.87
145d (DMSO)	+40°	91.92	167.06	60.45	23.69		24.26 (4',5') 31.45 (3',6') of cyclo-hexane
	-40°	91.69	166.66	60.01	23.59		24.08 (4',5') 31.24 (3',6') of cyclo-hexane

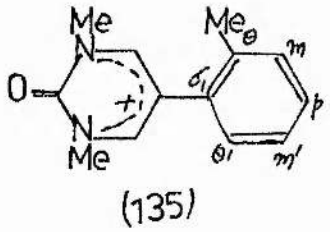


(146)

a, X=O, Z=H
b, X=S, Z=H
c, X=O, Z=OMe
d, X=S, Z=OMe
e, X=O, Z=NO_2
f, X=O, Z=Br

Table 15. ^{13}C N.m.r. Spectra of Salts (146a-f) in DMSO, Me_4Si Standard

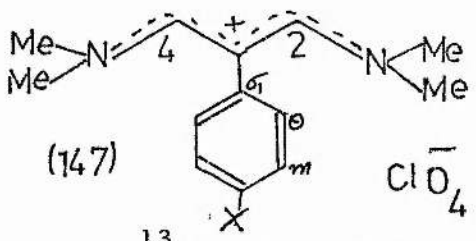
Compound	σ(5)	σ(4,6)	σ(2)	σ(others)
146a	116.13	158.02	147.24	1,3-Me,41.54; σ_1,130.15;o,125.96; m,129.23;p,128.87
146b	119.66	155.6-156.3br.	170.58	1,3-Me,48.26; σ_1,129.71; o,126.22;m,129.30;p,128.92
146c	116.06	157.47	147.18	1,3-Me,41.34;p-OMe,55.31; σ_1,122.34;o,127.34;m,114.72; p,159.84
146d	119.66	155.66	170.5 (br)	1,3-Me,48.3;p-OMe,55.31; σ_1, 121.76;o,127.65;m,114.87,p,160.39
146e	113.79	158.57	147.23	1,3-Me,41.69; σ_1,136.91;o, 127.04;m,124.34;p,147.38
146f	114.96	158.03	147.19	1,3-Me,41.82; σ_1,129.57;o,128.01; m,132.14;p,122.37



(135)

Table 16. ^{13}C N.m.r. Spectrum of the Compound (135) in DMSO, Me_4Si Standard

Compound	σ(5)	σ(4,6)	σ(2)	σ(others
135	116.61	159.66	147.42	1,3-Me,41.82;o-Me,19.53; σ_1, 130.28;o,136.33;m',126.48; o',m,p, 130.81/130.08/129.51

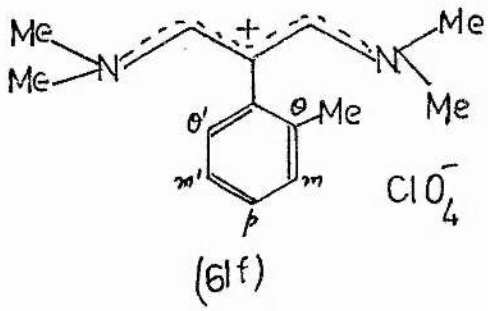


(147)

a, X=H
b, X=Me
c, X=Cl
d, X=NO_2

Table 17. ^{13}C N.m.r. Spectra of Salts (147) in DMSO, Me_4Si Standard

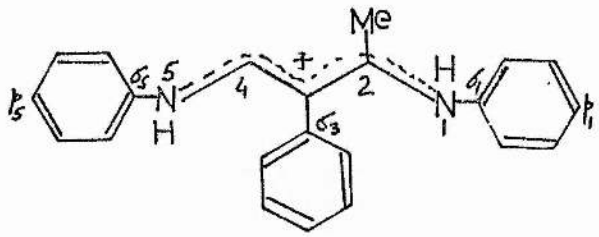
Compound	σ(Me)	σ(3)	σ(2,4)	σ(σ1)	σ(o)	σ(m)	σ(p)
147a	N-Me, 48.45	105.15	162.91	132.53	132.17	128.33	128.66
147b	N-Me, 48.38; p-Me, 20.75	105.11	163.10	129.39	132.01	128.94	138.08
147c	N-Me, 48.53	103.64	163.01	131.54	133.96	128.28	133.51
147d	N-Me, 48.60	102.57	162.81	140.46	133.30	123.08	147.27



(61f)

Table 18. ^{13}C N.m.r. of Salt (61f) in DMSO - Me_4Si Standard

σ(Me)	σ(3)	σ(2,3)	σ(σ1)	σ(o)	σ(o')	σ(m)+ (m')	σ(p)
N-Me, 48.40; o-Me, 19.82	103.59	162.83	131.97	138.58	132.34	129.23/129.79	125.83



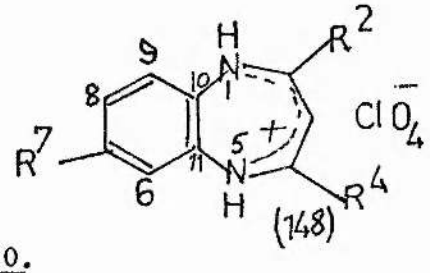
(82)

Table 19. ^{13}C N.m.r. Spectrum of salt (82) in Acetone Me_4Si Standard

σ(2-Me)	σ(3)	σ($\sigma_{1,5}$)	σ(σ_3)	σ(4)	σ(2)	σ(o_5)	σ(p_5)
17.22	112.34	137.63	140.17	152.62	174.59	119.66	126.55

σ(o_1)	σ(p_1)	σ($m_{1,5}$)	σ(m_3)	σ(p_3)	σ($m_{1,5}$)	σ(o_3)
127.22	129.33	130.14	130.31	131.08	131.33	132.51

^{13}C N.m.r. Spectra of 1,5-Benzodiazepinium Salts in DMSO (10% D_6)-Me_4Si Standard



(148)

a, R^2=R^4=Me
b, R^2=R^4=R^7=Me
c, R^2=R^4=Ph
d, R^2=R^4=Ph, R^7=Me

Table 20.

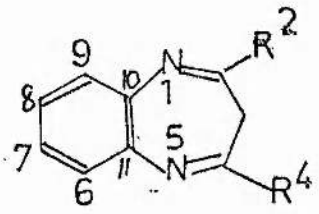
Compound	σ(2,4)	σ(3)	σ(Me)	σ(o)	σ(m)	σ(p)	σ(2,4)
148a	175.69	95.51	(2,4-Me) 24.05	-	-	-	-
148b	174.81 175.08	95.06	(2,4-Me), 24.01 (7-Me), 19.85	-	-	-	-
148c	174.43	95.52	-	128.06	128.92	134.51	136.15
148d	173.91 173.79	95.07	(7-Me), 19.99	128.03	128.96	134.48 134.63	135.99

(cont.)

Table 20. (cont.)

Compound	σ (7)	σ(8)	σ(10,11)	σ(6,9)
148a	129.13	129.13	133.79	123.44
148b	139.14	128.96	130.83(11) 133.58(10)	123.53(9) 123.98(6)
148c	129.52	129.52	133.74	125.43
148d	139.68	133.73	133.06(10) 129.49(11)	125.43(9) 125.99(6)

^{13}C N.m.r. Spectra of 1,5-Benzodiazepine Bases in DMSO-Me_4Si Standard



a, $R^2=R^4=Me$
b, $R^2=R^4=Ph$

(149)

Table 21.

Compound	σ(2,4)	σ(3)	σ(Me)	σ(o)	σ(m)	σ(p)	σ(2,4)
149a	157.59	43.22	27.54	-	-	-	-
149b	154.09	34.91	-	128.13	128.61	130.51	137.35

Compound	(7)	(8)	(10,11)	(6,9)
149a	127.55	127.55	140.34	124.86
149b	128.74	128.74	140.77	125.39

Table 22.

Compound	σ (meta)	σ (para)	$\lvert\sigma(m) - \sigma(p)\rvert$
140a	128.66	126.17	+ 2.49
140b	129.55	127.30	+ 2.25
140c	129.68	127.44	+ 2.24
140d	128.80	126.45	+ 2.35
140e	128.89	126.42	+ 2.47
140f	128.64 (6-m)	127.85 (6-p)	+ 1.79
140f	129.56 (1-m)	127.85 (1-p)	+ 1.71
140g	128.51 (6-m)	126.99 (6-p)	+ 1.52
140h	130.06	127.73	+ 2.33
140j	129.48	128.20	+ 1.28
140k	129.34	128.05	+ 1.29
89	129.84	132.56	- 1.72
77a	128.09	129.71	- 1.62
146a	129.23	128.87	+ 0.36
146b	129.30	128.92	+ 0.38

EXPERIMENTAL

Materials and Methods

Melting points were determined in open capillaries, and are uncorrected.

Unless otherwise stated, ultraviolet spectra are quoted for methanolic solutions: analytical samples were used.

Infrared spectra were recorded for nujol mulls.

Nmr spectra were recorded at 100 MHz for 10% solutions, with tetramethylsilane as internal reference. Sodium trimethylsilylpropanesulphonate was used as internal reference when deuterium oxide was the solvent.

Abbreviations

s = singlet

d = doublet

t = triplet

q = quartet

m = multiplet

b = broad

DMSO = dimethylsulphoxide

TFA = trifluoroacetic acid

TMS = tetramethylsilane

Vilsmeier formylations

(i) Preparation of 1,5-diaza-1,1,5,5-tetramethyl-1H-3-phenyl pentadienium perchlorate (24)

Phosphoryl chloride (27 ml, 0.3 mole) was added to cooled and stirred dimethylformamide (36.5 g, 0.5 mole), followed by phenylacetic acid (13.6 g, 0.1 mole). When the exothermic reaction had ceased, the mixture was heated and stirred at 80-90° until carbon dioxide ceased to evolve (ca. 3 hrs). The cooled reaction mixture was decomposed by ice (100 g) and an aqueous mixture was shaken with little charcoal, and filtered. The vinamidinium perchlorate was obtained in crystalline form by the addition of sodium perchlorate (14 g) to the filtrate. The product (20 g, 66%) was filtered off and washed with a little aqueous sodium perchlorate solution; it had mp. 212° (from ethanol), lit.[18] mp. 200-201° (from water).

(ii) 1,5-Diaza-1,1,5,5-tetramethyl-1H-3-p-nitrophenyl pentadienium perchlorate (61e)

3-p-Nitrophenyl vinamidinium perchlorate (25 g, 72%) was obtained by the same method as (i) above and had mp. 227° (from ethanol), lit.[73] mp. 225-226° (from methanol).

(iii) 1,5-Diaza-3-p-bromophenyl-1,1,5,5-tetramethyl-1H-pentadienium perchlorate (61b)

This salt (10.5 g, 60%) prepared from dimethylformamide (18.3 g), phosphoryl chloride (13.5 g) and p-bromophenylacetic acid (10.2 g) had mp. 130-132° (from ethanol), λ_{max} 316 nm (ε 35112), ν_{max} 1580, 1280, 1200, 1100, 800, 770, 760, 720 cm^{-1},

τ [($^2H_6$) DMSO], 2.24 (2H, s), 2.32-2.40 (2H, d), 2.66-2.75 (2H, d), 6.74 (6H, s), 7.53 (6H, s) (Found: C, 40.01; H, 4.85; N, 7.25 $C_{13}H_{18}BrClN_2O_4$ requires C, 40.91; H, 4.75; N, 7.34%).

(iv) 1,5-Diaza-3-p-chlorophenyl-1,1,5,5-tetramethyl-1H-pentadienium perchlorate (61a)

Phosphoryl chloride (27 ml, 0.3 mole) was added to cooled and stirred dimethylformamide (36.5 g, 0.5 mole), followed by p-chlorophenylacetic acid (17 g, 0.1 mole). The mixture was heated at 80-90° for 6 hrs, cooled and ice (100 g) was then added followed by a little charcoal. The mixture was filtered and sodium perchlorate (14 g) was added to the filtrate. This gave the crude vinamidinium perchlorate (22 g, 69%). The product had mp. 244-245° (from ethanol), λ_{max} 316 nm (ε 26976), ν_{max} 1570, 1280, 1190, 1100, 800, 760 cm^{-1}, τ [($^2H_6$)DMSO] 2.22 (2H, s), 2.45-2.54 (2H, d), 2.61-2.70 (2H, d), 6.74 (6H, s), 7.53(6H, s). (Found: C, 46.09; H, 5.46; N, 8.13 $C_{13}H_{18}Cl_2N_2O_4$ requires: C, 46.31; H, 5.38; N, 8.31%)

(v) 1,5-Diaza-1,1,5,5-tetramethyl-1H-3-p-tolyl pentadienium perchlorate (61d)

Phosphoryl chloride (13.5 ml, 0.15 mole) was slowly added to cooled, stirred dimethylformamide (18.2 g, 0.25 mole), followed by p-tolylacetic acid (7.5 g, 0.05 mole). The reaction mixture was heated at 80-90° for 4 hrs, cooled and poured onto ice (50 g); it was swirled with a little charcoal and finally filtered. Sodium perchlorate (7 g) was added to the filtrate and this gave colourless crystals which were filtered off and washed with a

little aqueous sodium perchlorate solution and finally with ether. The product (7.9 g, 50%) had mp. 150-152° (from ethanol), λ_{max} 316 nm (ε 49417), ν_{max} 1580, 1290, 1200, 1100, 810, 760, 720 cm^{-1}, τ [($^2H_6$Acetone], 2.20 (2H, s), 2.72 (4H, s), 6.65 (6H, s), 7.42 (6H, s), 7.62 (3H, s). (Found: C, 53.00; H, 6.70; N, 9.00 $C_{14}H_{21}ClN_2O_4$ requires: C, 53.08; H, 6.68; N, 8.84%)

(vi) 1,5-Diaza-1,1,5,5-tetramethyl-1H-3-o-tolyl pentadienium perchlorate (61f)

This salt was prepared by the same method as above (v); it had mp. 182-183° (from ethanol), λ_{max} 315 nm (ε 48150), ν_{max} 1590, 1290, 1210, 1100, 800, 750, 720 cm^{-1}, τ [TFA], 2.37 (2H, s), 2.62-2.78 (4H, m), 6.66 (6H, s), 7.46 (6H, s), 7.73 (3H, s). (Found: C, 52.87; H, 6.72; N, 9.07 $C_{14}H_{21}ClN_2O_4$ requires C, 53.08; H, 6.68; N, 8.84%)

(vii) 1,5-Diaza-3-p-methoxyphenyl-1,1,5,5-tetramethyl-1H-pentadienium perchlorate (61c)

The same method was used as in (v) in order to obtain this vinamidinium salt. The product (8.5 g, 51%) had mp. 126-127° (from ethanol), λ_{max} 316 nm (ε 40600), ν_{max} 1580, 1280, 1200, 1070, 800, 720 cm^{-1}, τ [($^2H_6$)Acetone], 2.20 (2H, s), 2.64-2.73 (2H, d), 2.93-3.02 (2H, d), 6.16 (3H, s), 6.65 (6H, s), 7.40 (6H, s). (Found: C, 50.50; H, 6.32; N, 8.32 $C_{14}H_{21}ClN_2O_5$ requires: C, 50.52; H, 6.36; N, 8.41%)

(viii) 1,5-Diaza-1,1,5,5-tetramethyl-1H-3-p-biphenyl pentadienium perchlorate (61g)

Vilsmeier reagent was prepared by adding phosphoryl chloride (7 ml) to cooled, stirred dimethylformamide (9.1 g). 4-Biphenyl acetic acid (5.3 g) was added to this mixture which was heated at 80-90° for 20 hrs. The mixture was decomposed by addition of ice (30 g) and the organic layer was extracted with chloroform (3 x 30 ml). The chloroform layer was dried over anhydrous sodium sulphate and the solution was concentrated in vacuo. This gave a heavy syrupy material to which methanol (5 ml) and perchloric acid (5 ml, 60%) were added. The brown rubbery material so obtained was triturated with water to give a solid which was filtered off and washed with ether. The product (5.6 g, 59%) had mp. 142-145°, λ_{max} 315 (ε 25762), ν_{max} 1580, 1290, 1210, 1100, 810, 750, 700 cm^{-1}, τ [($^2H_6$)DMSO] 2.21 (2H, s), 2.23-2.66 (9H, c, m), 6.75 (6H, s), 7.50 (6H, s). (Found: C, 59.81; H, 5.89; N, 7.10 $C_{19}H_{23}ClN_2O_4$ requires: C, 60.24; H, 5.89; N, 7.40%)

(ix) 1,5-Diaza-1,1,5,5-tetramethyl-3-α-naphthyl-1H-pentadienium perchlorate (61h)

This salt was prepared using the same method as that used above (i) for its phenyl analogue. It had mp. 189-190° (from ethanol), lit.[73] mp. 203-204° (from ethanol) λ_{max} 315 nm (ε 37928), ν_{max} 1580, 1290, 1210, 1100, 820, 720 cm^{-1}, τ [($^2H_6$)DMSO] 1.88 (2H, m), 1.92-2.45 (7H, m), 6.66-6.74 (6H, d), 7.45-7.84 (6H, d). (Found: C, 57.80; H, 6.00; N, 7.80 $C_{17}H_{21}ClN_2O_4$ requires: C, 57.87; H, 6.10; N, 7.90%)

(x) 1,5-Diaza-1,1,5,5-tetramethyl-3-β-naphthyl-1H-pentadienium perchlorate (61i)

Prepared by the same method as (i) above this salt (30 g, 85%) had m.p. 203-204° (from ethanol), λ_{max} 317 nm (ε 50806), ν_{max} 1590, 1290, 1210, 1100, 970, 820, 795, 770, 720 cm^{-1}, τ[($^2H_6$)DMSO], 1.93 (2H, m), 2.0-2.58 (7H, m), 6.66-6.72 (6H, d) 7.45-7.60 (6H, d) (Found: C, 57.23; H, 6.12; N, 7.80 $C_{17}H_{21}ClN_2O_4$ requires: C, 57.87; H, 6.10; N, 7.90%)

(xi) 3-Chloro-2-phenyl-but-2-enals

This compound was prepared by the literature method[66] and was used without further purification for the preparation of the following pentadienium perchlorate:

1,5-Diaza-1,5-diphenyl-2-methyl-3-phenyl-1H-pentadienium perchlorate

The unpurified sample of the chlorovinylaldehyde (11.7 g, 65 mmole) was dissolved in ethanol (50 ml). Aniline (25 g, 130 mmole) in ethanol (20 ml) was added to this stirred solution at room temperature followed, after ca 5 mins, by slow addition of perchloric acid (5.5 g). The yellow crystalline product (13.5 g, 50%) which formed after 30 mins was filtered off and washed well with ether. The product had m.p. 145-146°C, λ_{max} 360 nm and 280 nm (shoulder) (ε 23121), ν_{max} 3300, 1630, 1590, 1300, 1160, 1080, 750, 720, 690 cm^{-1}, τ[($^2H_6$)DMSO], 1.67-1.93 (1H, b, m), 2.30-2.83 (15H, m), 5.67-6.63 (NH, b), 7.53 (3H, s). (Found: C, 63.39; H, 5.91; N, 6.65 $C_{22}H_{21}ClN_2O_4$ requires: C, 65.00; H, 5.13; N, 6.78%)

(xii) 3-Chloro-2-methyl-4-phenyl-but-2-enals

Dimethylformamide (5.5 ml) was added to cooled phosphoryl chloride (5 ml) and the mixture was stirred for 30 mins in an ice bath. Benzyl ethyl ketone (5 ml) was added dropwise over a period of ca 30 mins to this mixture which was stirred further for 2 days. The complex was decomposed with ice and the product extracted with methylene chloride. The organic layer was washed successively with saturated aqueous sodium carbonate and with water. The product was finally dried over anhydrous sodium sulphate. Removal of the solvent in vacuo gave the crude chloro-vinylaldehyde (5.2 g, 79%), which was used to prepare the following vinamidinium salt.

1,5-Diaza-2-benzyl-3-methyl-1,5-diphenyl-1H-pentadienium perchlorate

Aniline (4.7 g, 50 mmoles) in ethanol (15 ml) was added to the unpurified chlorovinylaldhyde (4.9 g, 25 mmoles) in ethanol (10 ml). Slow addition of perchloric acid (2.5 g, 60%) to the mixture gave the pentadienium perchlorate after ca 15 mins. The product (3 g, 29%) was filtered off and washed well with ether. It had m.p. 167-168°, λ_{max} 340 nm and 305 nm (shoulder) (ε 34152) ν_{max} 3300, 1530, 1600, 1540, 1300, 1160, 1100, 750, 720, 690 cm^{-1}, τ [($^2H_6$)DMSO], 1.48-1.70 (1H, b, m), 2.51-2.99 (15H, c, m), 5.65 (2H, s), 6.20-6.60 (NH, b), 7.86 (3H, s). (Found: C, 64.76; H, 5.29; N, 6.52 $C_{23}H_{23}ClN_2O_4$ requires: C, 64.71; H, 5.43; N, 6.56%)

Preparation of N-(acetic)-pyridinium chloride

Pyridine (10.3 ml) was slowly added to a stirred solution of chloroacetic acid (9.4 g) in acetonitrile (50 ml). The mixture was warmed at 75-80°C for 45 mins and kept at room temperature overnight. Addition of ether gave a white powdery solid which was filtered off. It had m.p. 196° (decomp.).

(xiii) 1,5-Diaza-1,1,5,5-tetramethyl-1H-3-N-pyridinyl-pentadienium diperchlorate

Phosphoryl chloride (43 ml), followed by the pyridinium chloride (27.2 g), was added slowly to cooled, stirred dimethylformamide (58.4 g). The mixture was heated at 60-70° with stirring for 12 hrs and kept at room temperature overnight. The Vilsmeier compiex was cooled in an ice/salt mixture and decomposed by very slow addition of methanol (200 ml) with stirring. Perchloric acid (20 ml, 70%) was slowly added to the stirred mixture followed by ether (100 ml). The solid product (20 g, 32%) obtained was filtered off. It had m.p. 180-182°, λ_{max} 305 nm and 236 nm (shoulder) (ε 10442), ν_{max} 1620, 1300, 1200, 1100, 820, 800, 720 cm^{-1}, τ[($^2H_6$)Acetone], 0.73-0.80 (2H, d), 0.98-1.1 (1H, t), 1.56-1.63 (2H, d), 1.82 (2H, s), 6.62 (6H, s), 7.45 (6H, s). (Found: C, 34.58; H, 4.74; N, 9.99 $C_{12}H_{19}Cl_2N_3O_8$ requires: C, 35.66; H, 4.73; N, 10.39%). This was the best analysis which was obtained after repeated attempts although it provided the required dihydrodiazepinium salt satisfactorily.

Preparation of N-(acetic)-γ-picolyl chloride

This salt was prepared by the same method as its pyridyl analogue, and was used unpurified for the preparation of the following pentadienium salt:

(xiv) Attempted preparation of 1,5-diaza-1,1,5,5-tetramethyl-1H--N-picolyl pentadienium diperchlorate

The same method was used to prepare this salt as for its pyridyl analogue. The salt obtained had m.p. 170-180° (from acetonitrile/ether), λ_{max} 303 nm and 232 nm (shoulder) (ε 13038), ν_{max} 1620, 1400, 1300, 1200, 1170, 1100, 810, 780, 720 cm^{-1}, τ[($^2H_6$)DMSO] 0.92-1.16 (2H, b, m), 1.73-2.1 (4H, b, m), 6.61 (6H, s), 7.26 (3H, s), 7.46 (6H, s). (Found: C, 29.03; H, 4.15; N, 7.78 $C_{12}H_{21}Cl_2N_3O_8$ requires: C, 35.48; H, 5.21; N, 10.34%). This analysis represents C:H:N ratio 13:22:3.

Preparation of cyclic products from 1,5-diaza-1,1,5,5-tetramethyl-1H-3-phenyl pentadienium perchlorate

Reactions with 1,2-diamines

Typical procedure:

2,3-Dihydro-6-phenyl-1H-1,4-diazepinium perchlorate (62a)

Ethylenediamine (0.27 g, 4.5 mmoles) in methanol (10 ml) was added in one portion to the pentadienium perchlorate (1.36 g, 4.5 mmoles) in methanol (150 ml), and the mixture was heated under reflux for ca 20 mins. Evaporation of the solvent in vacuo gave crystals of dihydrodiazepinium perchlorate. Crystallised from ethanol (1.1 g, 89%), it had m.p. 177-178°, λ_{max} 352 and 246 nm (ε 7400 and 10900), ν_{max} 3300, 1620, 1530, 1310, 1100 cm^{-1},

τ[TFA], 1.5-1.86 (2H, b), 2.06-2.14 (2H, d), 2.58-2.82 (5H, m), 6.0-6.18 (4H, m). (Found: C, 48.4; H, 4.9; N, 10.2 $C_{11}H_{13}ClN_2O_4$ requires: C, 48.45; H, 4.75; N, 10.3%)

The following dihydrodiazepinium salts were prepared by the same method:

2,3-Dihydro-1,4-dimethyl-6-phenyl-1H-1,4-diazepinium perchlorate (62b)

This salt (0.73 g, 82%), prepared by heating a mixture of the pentadienium perchlorate (0.82 g, 3 mmoles) and N,N'-dimethylethylenediamine (0.27 g, 3 mmoles) in methanol (110 ml) under reflux for ca $2\frac{1}{2}$ hrs, had m.p. 154-156° (from ethanol) λ_{max} 367 and 253 nm (ε 12160 and 12814) ν_{max} 1640, 1560, 1330, 1250, 1100 cm^{-1}, τ[($^2H_6$)DMSO], 2.02 (2H, s), 2.65 (5H, s), 6.2 (4H, s), 6.51 (6H, s). (Found: C, 51.86; H, 5.84; N, 9.44 $C_{13}H_{17}ClN_2O_4$ requires: C, 51.87; H, 5.65; N, 9.31%)

2,3-Dihydro-1-methyl-6-phenyl-1H-1,4-diazepinium perchlorate (62c)

This salt (2.5 g, 88%), prepared by heating a methanolic solution of the pentadienium perchlorate (3 g, 10 mmoles) and N-methylethylenediamine (0.7 g, 10 mmoles) under reflux for $1\frac{1}{2}$ hrs, had m.p. 150-151° (from ethanol), λ_{max} 363 and 251 nm (ε 10240 and 12698), ν_{max} 3300, 1640, 1540, 1350, 1100 cm^{-1}, τ[($^2H_6$)Acetone], 1.95-1.99 (2H, m), 2.62 (5H, s), 6.02 (4H, s), 6.32 (3H, s). (Found: C, 50.22; H, 5.23; N, 9.77 $C_{12}H_{15}ClN_2O_4$ requires: C, 50.12; H, 5.37; N, 9.81%)

2,3-Dihydro-2-methyl-6-phenyl-1H-1,4-diazepinium perchlorate (62d)

Prepared from the pentadienium perchlorate (3 g, 10 mmoles) and 1,2-diaminopropane (0.7 g, 10 mmoles), this salt

(2.4 g, 86%) had m.p. 105° (from ethanol), λ_{max} 353 and 245 nm (ε 7979 and 12217), ν_{max} 3300, 1640, 1550, 1340, 1100 cm^{-1}, τ[($^2H_6$)Acetone], 1.86 (1H, d), 1.97 (1H, d), 2.63(5H, s), 5.60-5.86 (1H, b), 6.16 (2H, d), 8.56-8.63 (3H, d). (Found: C, 50.07; H, 5.36; N, 9.79 $C_{12}H_{15}ClN_2O_4$ requires: C, 50.22; H, 5.23; N, 9.77%)

2,3-Dihydro-2,2-dimethyl-6-phenyl-1H-1,4-diazepinium perchlorate (62e)

This salt (1.8 g, 60%), prepared by heating a methanolic solution of the pentadienium perchlorate (3 g, 10 mmoles) and 1,2-diamino-2-methylpropane (0.9 g, 10 mmoles) under reflux for ca 3 hrs, had m.p. 156-158° (from ethanol), λ_{max} 352 and 246 nm (ε 6799 and 10460), ν_{max} 3300, 1640, 1520, 1360, 1100 cm^{-1}, τ[($^2H_6$)Acetone], 0.05-0.5 (2H, b), 1.76-1.90 (1H, b), 1.98-2.12 (1H, b, d), 2.62 (5H, s), 6.2-6.46 (2H, b), 8.54 (6H, s). (Found: C, 51.81; H, 5.71; N, 9.54 $C_{13}H_{17}ClN_2O_4$ requires: C, 51.87; H, 5.65; N, 9.31%)

2,3-Cyclohexano-2,3-dihydro-6-phenyl-1H-1,4-diazepinium perchlorate (62g)

A methanolic solution of the pentadienium perchlorate (1.2 g, 4 mmoles) and of 1,2-diaminocyclohexane (0.46 g, 4 mmoles) was heated under reflux for ca 8 hrs, and the crystals (1 g, 74%) which resulted after working up the reaction mixture had m.p. 226-227° (from ethanol), λ_{max} 355 and 247 nm (ε 8627 and 14509), ν_{max} 3300, 1640, 1500, 1370, 1100 cm^{-1}, τ[($^2H_6$)DMSO], -0.6- 0 (2H, b), 2.22 (2H, s), 2.62 (5H, s), 6.6-6.88 (2H, b, m), 8.06-8.82 (8H, b, c, m). (Found: C, 54.89; H, 6.01; N, 8.41

$C_{15}H_{19}ClN_2O_4$ requires: C, 55.09; H, 5.82; N, 8.57%)

1,4-Dibenzyl-2,3-dihydro-6-phenyl-1H-1,4-diazepinium perchlorate (62f)

Prepared from a methanolic solution of the pentadienium perchlorate (1.5 g, 5 mmoles) and N,N'-dibenzylethylenediamine (1.2 g, 5 mmoles) which was heated under reflux for 3 hrs, this salt (1.83 g, 82%) had m.p. 218-222° (from acetonitrile), λ_{max} 372 and 253 nm, (ε 13022 and 17929), ν_{max} 1640, 1590, 1550, 1340, 1100 cm^{-1}, τ [TFA] 1.97 (2H, s), 2.54-2.65 (15H, c, m), 5.13 (4H, s), 6.26-6.52 (4H, b). (Found: C, 66.08 ; H, 5.89; N, 6.11 $C_{25}H_{25}ClN_2O_4$ requires: C, 66.23; H, 5.52; N, 6.18%

Product from a reaction of the pentadienium perchlorate and piperazine

The product obtained (1.28 g, 81%) by heating a methanolic solution of the pentadienium perchlorate (1.5 g, 5 mmoles) and piperazine hydrate (1 g, 5 mmoles) under reflux for 1 hr had m.p. 152-155° (decomp.) from ethanol, and mixed m.p. with the pentadienium perchlorate 142-174°. The product could not be identified by its ^1H nmr and the microanalysis. (Found: C, 51.91; H, 6.66; N, 11.02, which represents C:H:N ratio 11:17:2)

Preparation of dihydrodiazepinium salts using p-substituted 3-aryl vinamidinium salts

(a) Preparation of cyclic products from 1,5-diaza-1,1,5,5-tetramethyl-1H-3-p-tolyl pentadienium perchlorate

2,3-Dihydro-6-p-tolyl-1H-1,4-diazepinium perchlorate (63a)

Ethylenediamine (0.3 g, 5 mmoles) in methanol (10 ml) was added in one portion to the pentadienium perchlorate (1.58 g, 5 mmoles)

dissolved in methanol (30 ml). The mixture was heated under reflux for 1 hr, concentrated in vacuo, and this gave crystals (1.2 g, 84%) which had m.p. 206-210° (from ethanol), λ_{max} 358 and 248 nm (ε 6758 and 14335), ν_{max} 3300, 1640, 1550, 1350, 1100, 820 cm^{-1}, τ [($^2H_6$)Acetone], 2.0-2.09 (2H, d), 2.80 (4H, s), 6.20-6.34 (4H, b, m), 7.69 (3H, s). (Found: C, 50.84; H, 5.28; N, 9.48 $C_{12}H_{15}ClN_2O_4$ requires: C, 50.27; H, 5.27; N, 9.78%)

2,3-Dihydro-1,4-methyl-6-p-tolyl-1H-1,4-diazepinium perchlorate(63b)

N,N'-Dimethylethylenediamine (0.18 g, 2 mmoles) in methanol (2 ml) was added to the pentadienium salt (0.63 g, 2 mmoles) dissolved in methanol (30 ml). The mixture was heated under reflux for 2 hrs, and removal of solvent in vacuo yielded product (0.5 g, 80%), which had m.p. 180-182° (from ethanol), λ_{max} 370 and 254 nm (ε 9789 and 12943), ν_{max} 1640, 1570, 1380, 1100, 830 cm^{-1}, τ [($^2H_6$)DMSO], 2.05 (2H, s), 2.79 (4H, s), 6.23 (4H, s), 6.54 (6H, s), 7.72 (3H, s). (Found: C, 53.63; H, 6.64; N, 8.27 $C_{14}H_{19}ClN_2O_4$ requires: C, 53.52; H, 6.07; N, 8.88%)

2,3-Dihydro-1-methyl-6-p-tolyl-1H-1,4-diazepinium perchlorate

The salt (1.2 g, 80%), prepared from a methanolic solution of the pentadienium salt (1.58 g, 5 mmoles) and N-methylethylenediamine (0.37 g, 5 mmoles) by heating it under reflux for 3 hrs, had m.p. 118-120° (from ethanol), λ_{max} 366 and 252 nm (ε 9604 and 14552), ν_{max} 3300, 1640, 1550, 1370, 1100, 830 cm^{-1}, τ [($^2H_6$)Acetone/TFA], 1.86 (2H, s), 2.76 (4H, s), 6.0 (4H, m), 6.33 (3H, s), 7.67 (3H, s). (Found: C, 51.26; H, 5.78; N, 9.13 $C_{13}H_{17}ClN_2O_4$ requires: C, 51.92; H, 5.70; N, 9.31%)

2,3-Dihydro-2-methyl-6-p-tolyl-1H-1,4-diazepinium perchlorate

Prepared from a methanolic solution of the vinamidinium perchlorate (1.58 g, 5 mmoles) and 1,2-diaminopropane (0.37 g, 5 mmoles) by heating it under reflux for 4 hrs, this salt (1.4 g, 93%) had m.p. 180-181° (from ethanol), λ_{max} 358 and 248 nm (ε 8110 and 15492), ν_{max} 3300, 1540, 1590, 1380, 1100, 820 cm^{-1}, τ [($^2H_6$)DMSO], 2.05 (1H, d), 2.18 (1H, d), 2.80 (4H, s), 5.85-6.2 (1H, b), 6.44 (2H, m), 7.69 (3H, s), 8.74-8.8 (3H, d). (Found: C, 51.86; H, 5.85; N, 9.15 $C_{13}H_{17}ClN_2O_4$ requires: C, 51.92; H, 5.70; N, 9.31%)

2,3-Cyclohexano-2,3-dihydro-6-p-tolyl-1H-1,4-diazepinium perchlorate

This salt was prepared by heating under reflux a solution of 1,2-diaminocyclohexane (1.14 g, 10 mmoles)in methanol (70 ml) for ca 6 hrs. Removal of the solvent gave crystals (1.4 g, 41%) which had m.p. 208-210° (from ethanol), λ_{max} 360 and 248 nm (ε 8179 and 17040), ν_{max} 3300, 1640, 1520, 1370, 1100, 820 cm^{-1}, τ [($^2H_6$)DMSO], 0.06-0.4 (2H, b), 2.17-2.25 (2H, c, d), 2.80 (4H, s), 6.6-6.8 (2H, b), 7.68 (3H, s), 8.02-8.6 (8H, b, c, m). (Found: C, 56.07; H, 6.37; N, 7.99 $C_{16}H_{21}ClN_2O_4$ requires: C, 56.39; H, 6.21; N, 7.55%)

1,4-Dibenzyl-2,3-dihydro-6-p-tolyl-1H-1,4-diazepinium perchlorate

N,N'-Dibenzylethylenediamine (0.63 g, 3 mmoles) in methanol (5 ml) was added to the pentadienium perchlorate (0.95 g, 3 mmoles) dissolved in methanol (40 ml). The mixture was heated under reflux for 6 hrs. The mixture was allowed to cool and this

gave yellow crystals (1 g, 76%) which were filtered off and washed with ether. The product had m.p. 178° (from acetonitrile), λ_{max} 360 and 248 nm (ε 13619 and 31520), ν_{max} 1630, 1540, 1370, 1100, 820 cm^{-1}, τ [($^2H_6$)DMSO] 1.66 (2H, s), 2.59 (10H, s), 2.67-2.70 (4H, d), 5.05 (4H, s), 6.42 (4H, s), 7.66 (3H, s). (Found: C, 66.47; H, 5.45; N, 5.96 $C_{26}H_{27}ClN_2O_4$ requires: C, 66.81; H, 5.78; N, 5.99%)

(b) Preparation of cyclic products from 1,5-diaza-1,1,5,5-tetramethyl-1H-3-p-anisyl pentadienium perchlorate

6-p-Anisyl-2,3-dihydro-1H-1,4-diazepinium perchlorate

Ethylenediamine (0.6 g, 10 mmoles) in methanol (10 ml) was added to thepentadienium perchlorate (3.3 g, 10 mmoles) dissolved in methanol (100 ml). The mixture was heated under reflux for 1 hr, the solvent was removed in vacuo, and the crystalline product (2.86 g, 95%) was filtered off; it had m.p. 204-208° (from ethanol), λ_{max} 362 and 248 nm (ε 5865 and 12865), ν_{max} 3300, 1640, 1370, 1100, 850, 820 cm^{-1}, τ [($^2H_6$)Acetone], 2.04 (2H, s), 2.66-2.75 (2H, d), 2.98-3.07 (2H, d), 6.14 (4H, s), 6.20 (3H, s). (Found: C, 47.82; H, 5.03; N, 9.67 $C_{12}H_{15}ClN_2O_5$ requires: C, 47.57; H, 4.96; N, 9.25%)

6-p-Anisyl-2,3-dihydro-2-methyl-1H-1,4-diazepinium perchlorate

Prepared from a methanolic solution of the pentadienium perchlorate (3.3 g, 10 mmoles) and 1,2-diaminopropane (0.75 g, 10 mmoles) by heating it under reflux for 5 hrs, this salt (2.6 g, 86%) had m.p. 174-176° (from ethanol), λ_{max} 376 and 253 nm,

(ε 7523 and 9502), ν_{max} 3300, 1540, 1370, 1100, 830 cm^{-1}, τ [($^2H_6$)DMSO], 2.09-2.21 (2H, d), 27.1-2.80 (2H, d), 3.0-3.1 (2H, d), 5.80-6.1 (1H, b, m), 6.24 (3H, s), 6.46 (2H, b), 8.74-8.81 (3H, d). (Found: C, 49.23; H, 5.39; N, 8.77 $C_{13}H_{17}ClN_2O_5$ requires: C, 49.25; H, 5.37; N, 8.84%)

6-p-Anisyl-2,3-dihydro-2,2-dimethyl-1H-1,4-diazepinium perchlorate

Prepared from the pentadienium perchlorate (3.3 g, 10 mmoles) and 1,2-diamino-2-methylpropane (0.9 g, 10 mmoles), this salt (3.3 g, 91%) had m.p. 137-138° (from ethanol), λ_{max} 360 and 247 nm (ε 6812 and 16739), ν_{max} 3300, 1540, 1350, 1100, 840, 820 cm^{-1}, τ [($^2H_6$)DMSO] 2.0 (1H, d), 2.3 (1H, d), 2.62-2.80 (2H, d), 2.93-3.2 (2H, d), 6.2 (3H, s), 6.6 (2H, s), 8.65 (6H, s). (Found: C, 50.70; H, 5.77; N, 8.61 $C_{14}H_{19}ClN_2O_4$ requires: C, 50.79; H, 5.74; N, 8.47%)

6-p-Anisyl-1,4-dibenzyl-2,3-dihydro-1H-1,4-diazepinium perchlorate

1,2-Dibenzylethylenediamine (2.1 g, 10 mmoles) was added to a methanolic solution of the pentadienium perchlorate (3.3 g, 10 mmoles). The mixture was heated under reflux for 4 hrs, the solvent was removed in vacuo, and the crystalline product (2.6 g, 51.6%) was filtered off and finally was washed with ether. The product had m.p. 174-176° (from ethanol), λ_{max} 380 and 253 nm (ε 12139 and 18797), ν_{max} 1640, 1350, 1100, 840, 820 cm^{-1},

τ [($^2H_6$)Acetone], 1.76 (2H, s), 2.57 (10H, d), 2.61-2.66 (2H, d), 2.80-3.07 (2H, d), 4.96 (4H, s), 6.2) (4H, s), 6.25 (3H, s). (Found: C, 64.47; H, 5.55; N, 5.74 $C_{26}H_{27}ClN_2O_5$ requires: C, 64.60; H, 5.59; N, 5.79%)

(c) Cyclisation of 1,5-diaza-1,1,5,5-tetramethyl-1H-3-p-nitrophenyl pentadienium perchlorate

2,3-Dihydro-6-p-nitrophenyl-1H-1,4-diazepinium perchlorate

Ethylenediamine (0.6 g, 10 mmoles) in methanol (20 ml) was added to the methanolic solution of the p-nitrophenyl pentadienium perchlorate (3.4 g, 10 mmoles). The mixture was heated under reflux for 15 mins, and the solvent was removed in vacuo. A crystalline product (2.8 g, 72%) so obtained was filtered off and washed with ether. It had m.p. 192° (from ethanolic perchloric acid), λ_{max} 345 nm (ε 18304), ν_{max} 3300, 1640, 1560, 1330, 1230, 1100, 910, 850, 700 cm^{-1}, τ [($^2H_6$)DMSO] 1.67-1.77 (2H, d), 1.82 (2H, s), 2.30-2.41 (2H, d), 6.15 (4H, m). (Found: C, 41.72; H, 3.85; N, 13.28 $C_{11}H_{12}ClN_3O_6$ requires C, 41.59; H, 3.81; N, 13.23%)

2,3-Dihydro-1,4-dimethyl-6-p-nitrophenyl-1H-1,4-diazepinium perchlorate

This salt, prepared from the corresponding vinamidinium perchlorate (1.3 g, 4 mmoles) in methanol (50 ml) and N,N'-dimethylethylenediamine (0.36 g, 4 mmoles) in methanol (20 ml), had m.p. 161-162°C (from ethanol), λ_{max} 356 nm (ε 20250), ν_{max} 1640, 1560, 1330, 1220, 1100, 910, 850, 720 cm^{-1}, τ [($^2H_6$)DMSO] 1.72-1.82 (2H, d), 1.84 (2H, s), 2.30-2.39 (2H, d),

6.13 (4H, s), 6.45 (6H, s). (Found: C, 45.30; H, 4.70; N, 12.14 $C_{13}H_{16}ClN_3O_6$ requires: C, 45.16; H, 4.66; N, 12.15%)

1,4-Dibenzyl-2,3-dihydro-6-p-nitrophenyl-1H-1,4-diazepinium perchlorate

This salt was prepared similarly by heating under reflux for 4 hrs a mixture of the corresponding vinamidinium perchlorate and N,N'-dibenzylethylenediamine in methanol. It had m.p. 162° (from acetonitrile), λ_{max} 364 nm (ε22790), ν_{max} 1630, 1580, 1560, 1330, 1250, 1100, 850, 720 cm^{-1}, τ[($^2H_6$)DMSO], 1.46 (2H, s), 1.62-1.75 (2H, d), 2.16-2.30 (2H, d), 2.57 (10H, s), 5.03 (4H, s), 6.37 (4H, s). (Found: C, 60.57, H, 4.42; N, 8.32 $C_{25}H_{24}ClN_3O_6$ requires:C, 60.30; H, 4.86; N, 8.44%)

(d) Cyclisation of 1,5-diaza-3-p-chlorophenyl-1,1,5,5-tetramethyl-1H-pentadienium perchlorate

6-p-Chlorophenyl-2,3-dihydro-1H-1,4-diazepinium perchlorate

The corresponding pentadienium perchlorate (1.6 g, 5 mmoles) was dissolved in methanol (100 ml), and ethylenediamine (0.3 g, 5 mmoles) in methanol (20 ml), was added to this solution. The mixture was heated under reflux for 1 hr. Removal of the solvent in vacuo gave the product which was filtered off and washed with ether. The product (1.1 g, 76%) had m.p. 140° (from ethanol), λ_{max} 354 and 255 nm (ε 9828 and 20393), ν_{max} 3300, 1640, 1550, 1320, 1230, 1100, 1040, 920, 830, 720 cm^{-1}, τ[($^2H_6$)DMSO]+TFA, 1.98-2.07 (2H, d), 2.61 (4H, s), 6.25 (4H, b). (Found: C, 42.95; H, 3.85; N, 8.99 $C_{11}H_{12}Cl_2N_2O_4$ requires: C, 43.01; H, 3.93; N, 9.12%)

(e) Cyclisation of 1,5-diaza-3-p-bromophenyl-1,1,5,5-tetramethyl-1H-pentadienium perchlorate

6-p-Bromophenyl-2,3-dihydro-1H-1,4-diazepinium perchlorate

Ethylenediamine (0.3 g, 5 mmoles) in methanol (20 ml) was added in one portion to the pentadienium perchlorate (1.9 g, 5 mmoles) dissolved in methanol (60 ml). The mixture was heated under reflux for 1 hr. Removal of the solvent in vacuo gave crystals which were filtered off and washed with ether. The product (1.9 g, 91%) was identified by its m.p. and mixed m.p. with the authentic sample.

(f) Cyclisation of 1,5-diaza-1,1,5,5-tetramethyl-1H-3-p-biphenyl pentadienium perchlorate

2,3-Dihydro-6-p-biphenyl-1H-1,4-diazepinium perchlorate

Ethylenediamine (0.2 g, 3mmoles) in methanol (20 ml) was added in one portion to a methanolic solution of the p-biphenyl pentadienium perchlorate (1.1 g, 3 mmoles). The mixture was heated under reflux for 20 mins, and removal of the solvent in vacuo gave a crystalline product (0.9 g, 89%) which had m.p. 295° (decomp.) (from acetonitrile), λ_{max} 360 and 275 nm (ε 7363 and 31778), ν_{max} 3300, 1630, 1530, 1300, 1200, 1100, 910, 830, 770, 720 cm^{-1}, τ [($^2H_6$)DMSO], 1.96 (2H, d), 2.27-2.64 (9H, c, m), 6.2-6.24 (4H, m). (Found: C, 58.53; H, 4.69; N, 7.79 $C_{17}H_{17}ClN_2O_4$ requires: C, 58.54; H, 4.90; N, 8.03%)

(g) Cyclisation of 1,5-diaza-1,1,5,5-tetramethyl-1H-3-α-naphthyl pentadienium perchlorate

2,3-Dihydro-6-α-naphthyl-1H-1,4-diazepinium perchlorate

Ethylenediamine (0.6 g, 10 mmoles) in ethanol(20 ml) was added to the pentadienium perchlorate (3.5 g, 10 mmoles) dissolved in ethanol (60 ml) and the mixture was heated under reflux for 30 mins. When the cyclisation was found to be complete, by monitoring the reaction by means of uv spectroscopy, removal of the solvent in vacuo gave a thick golden syrup which when cooled was triturated with ether. The powdered solid (3.2 g, 99%) which was filtered off had m.p. 100-102° (from acetonitrile, λ_{max} 350 and 293 nm (ε 8176 and 9467), ν_{max} 3300, 1635, 1540, 1320, 1230, 1100, 950, 920, 770, 710 cm^{-1}, τ[TFA] 2.04-2.08 (2H, d), 2.41-2.60 (7H, c, m), 6.00 (4H, s). (Found: C, 55.98; H, 5.07; N, 8.98 $C_{15}H_{15}ClN_2O_4$ requires: C, 55.82; H, 4.70; N, 8.68%)

2,3-Dihydro-1,4-dimethyl-6-α-naphthyl-1H-1,4-diazepinium perchlorate

The pentadienium perchlorate (3.5 g, 10 mmoles) was dissolved in methanol (60 ml). N,N'-Dimethylethylenediamine (0.9 g, 10 mmoles) in methanol was added, and the mixture was heated under reflux for 7 hrs. The solvent was removed in vacuo and the residue was kept in the refrigerator overnight and gave the solid product which was filtered off and finally washed with ether. The product (3.2 g, 92%) had m.p. 139-140° (from ethanol), λ_{max} 364 and 295 nm (ε 11776 and 9772), ν_{max} 1635, 1560, 1320, 1140, 1080, 935, 785, 715 cm^{-1}, τ[($^2H_6$)DMSO] 1.98 (2H, s), 2.02-2.56 (7H, c, m), 6.07 (4H, s), 6.57 (6H, s). (Found: C, 57.92; H, 5.38, N, 7.91 $C_{17}H_{19}ClN_2O_4$ requires: C, 58.21; H, 5.46; N, 7.99%)

2,3-Dihydro-1-methyl-6-α-naphthyl-1H-1,4-diazepinium perchlorate

A mixture of the pentadienium salt and N-methylethylenediamine in methanol was heated under reflux for 6 hrs. The residue left after removal of the solvent in vacuo was triturated in ether to give the solid which was filtered off. It had m.p. 94-96°, λ_{max} 358 and 294 nm (ε 9787 and 9261), ν_{max} 3300, 1635, 1550, 1320, 1100, 925, 840, 780, 720 cm^{-1}, τ [($^2H_6$)DMSO] 1.80 (1H, d), 1.95 (1H, s), 2.02-2.54 (7H, c, m), 6.20 (4H, s), 6.45 (3H, s). (Found: C, 57.78; H, 5.07; N, 7.86 $C_{18}H_{17}ClN_2O_4$ requires: C, 57.06; H, 5.08; N, 8.32%)

1,4-Dibenzyl-2,3-dihydro-6-α-naphthyl-1H-1,4-diazepinium perchlorate

This compound (1.6 g, 75%), prepared by heating a methanolic solution of the pentadienium perchlorate (1.7 g, 5 mmoles) and N,N'-dibenzylethylenediamine (1.2 g, 5 mmoles) under reflux for 4 hrs had m.p. 92-94°, λ_{max} 368 and 310 nm (ε 9278 and 17486), ν_{max} 1630, 1550, 1070, 720 cm^{-1}, τ [($^2H_6$)DMSO] 1.79 (2H, s), 1.94-2.44 (7H, c, m), 2.60 (10H, s), 5.11 (4H, s), 6.2-6.3 (4H, b). (Found: C, 65.22; H, 5.53; N, 5.99 $C_{29}H_{25}ClN_2O_4$ requires: C, 69.24; H, 5.47; N, 5.57%). This was the best analysis which was obtained despite repeated attempts.

(h) Cyclisation of 1,5-diaza-1,1,5,5-tetramethyl-1H-3-β-naphthyl-pentadienium perchlorate

2,3-Dihydro-6-β-naphthyl-1H-1,4-diazepinium perchlorate

Ethylenediamine (0.3 g, 5 mmoles) in methanol (20 ml)

was added to the corresponding pentadienium perchlorate (1.7 g, 5 mmoles), dissolved in methanol (60 ml). The mixture was heated under reflux for 30 mins. Removal of the solvent in vacuo gave a crystalline product which was filtered off and washed with ether. The product (1.4 g, 90%) had m.p. 168-170° (from ethanol), λ_{max} 355 and 297 nm (shoulder) (ε 7531), ν_{max} 3300, 1635, 1540, 1320, 1220, 1100, 920, 860, 820, 750 cm^{-1}, τ[($^2H_6$)DMSO], 1.89 (2H, s), 2.02-2.54 (7H, c, m), 6.22 (4H, s). (Found: C, 55.52; H, 4.84; N, 8.57 $C_{15}H_{15}ClN_2O_4$ requires: C, 55.82; H, 4.70; N, 8.68%)

2,3-Dihydro-1,4-dimethyl-6-β-naphthyl-1H-1,4-diazepinium perchlorate

A mixture of the pentadienium perchlorate (1.7 g, 5 mmoles) and N,N'-dimethylethylenediamine (0.45 g, 5 mmoles) in methanol (80 ml) was heated under reflux for 6 hrs. Removal of the solvent gave crystals (1.5 g, 89%) which were filtered off, and had m.p. 184° (from ethanol), λ_{max} 370 and 286 nm (ε 10758 and 12746), ν_{max} 1630, 1570, 1250, 1080, 900, 860, 830, 750 cm^{-1}, τ[($^2H_6$)DMSO], 1.86 (2H, s), 2.0-2.50 (7H, c, m), 6.16 (4H, s), 6.47 (6H, s). (Found: C, 58.41; H, 5.42, N, 7.93 $C_{17}H_{19}ClN_2O_4$ requires: C, 58.21; H, 5.46; N, 7.99%)

2,3-Dihydro-1-methyl-6-β-naphthyl-1H-1,4-diazepinium perchlorate

N-Methylethylenediamine (0.4 g, 5 mmoles) in methanol (20 ml) was added in one portion to the pentadienium perchlorate (1.7 g, 5 mmoles) dissolved in methanol (60 ml). The mixture was heated under reflux for 6 hrs, solvent was removed in vacuo, and the

resultant crystalline product (0.8 g, 49%) was filtered off. It had m.p. 105° (from ethanol), λ_{max} 364 nm (ε 7930), ν_{max} 3300, 1640, 1550, 1320, 1240, 1160, 1100, 925, 890, 850, 745 cm^{-1}, τ [($^2H_6$)DMSO] 1.81 (1H, d), 1.94 (1H, d), 2.02-2.54 (7H, c, m), 6.20 (4H, s), 6.45 (3H, s). (Found: C, 56.86; H, 5.28; N, 8.07 $C_{16}H_{17}ClN_2O_4$ requires: C, 57.06; H, 5.10; N, 8.31%)

2,3-Dihydro-2,2-dimethyl-6-β-naphthyl-1H-1,2-diazepinium perchlorate

A mixture of the pentadienium perchlorate (1.7 g, 5 mmoles) and 1,2-diamino-2-methylpropane (0.45 g, 5 mmoles) in methanol (80 ml) was heated under reflux for 7 hrs. The solvent was removed in vacuo, and the thick oily residue readily gave crystals when cooled. The product (1.4 g, 83%) was filtered off and had m.p. 191-192° (from ethanol), λ_{max} 358 nm (ε 7276), ν_{max} 3280, 1630, 1520, 1320, 1100, 950, 890, 860, 815, 750 cm^{-1}, τ [($^2H_6$)DMSO] 1.82 (1H, d), 1.97 (1H, d), 2.02-2.56 (7H, c, m), 6.53 (2H, b), 8.64 (6H, s). (Found: C, 57.90; H, 5.36; N, 7.87 $C_{17}H_{19}ClN_2O_4$ requires: C, 58.21; H, 5.45; N, 7.98%)

1,4-Dibenzyl-2,3-dihydro-6-β-naphthyl-1H-1,4-diazepinium perchlorate

Prepared by heating under reflux for 7 hrs a mixture of N,N'-dibenzylethylenediamine (1.2 g, 5 mmoles) and the pentadienium perchlorate (1.7 g, 5 mmoles) in methanol (80 ml), this yellow crystalline salt had m.p. 182-184° (from acetonitrile), λ_{max} 376 nm (ε 12651), ν_{max} 1630, 1550, 1200, 1080, 720 cm^{-1},

τ [($^2H_6$)DMSO], 1.45 (2H, s), 2.0-2.52 (7H, c, m), 2.56 (10H, s), 5.0 (4H, s), 6.38 (4H, b). (Found: C, 69.40; H, 5.48; N, 5.35 $C_{29}H_{27}ClN_2O_4$ requires: C, 69.23; H, 5.41; N, 5.57%)

2,3-Cyclohexano-2,3-dihydro-6-β-naphthyl-1H-1,4-diazepinium perchlorate

A methanolic solution of the pentadienium perchlorate (1.7 g, 5 mmoles) and of 1,2-diaminocyclohexane (0.6 g, 5 mmoles) was heated under reflux for 6 hrs. The solvent was removed in vacuo and the resultant residue was cooled and triturated with ether. The solid product which formed was filtered off and had m.p. 198-200° λ_{max} 360 nm (ε 6596), ν_{max} 3280, 1620, 1100, 860, 820, 730 cm^{-1}, τ [($^2H_6$)DMSO], 2.0-2.60 (9H, c, m), 6.60-6.80 (2H, b, m), 8.2-8.8 (8H, b, c, m). (Found: C, 60.43; H, 5.58; N, 7.41 $C_{19}H_{21}ClN_2O_4$ requires: C, 60.56; H, 5.61; N, 7.43%)

(i) Cyclisation of 1,5-diaza-1,1,5,5-tetramethyl-1H-3-N-pyridyl pentadienium diperchlorate

2,3-Dihydro-6-N-pyridyl-1H-1,4-diazepinium diperchlorate

Ethylenediamine (0.64 g, 10 mmoles) in ethanol (20 ml) was added to the N-pyridyl pentadienium diperchlorate (4 g, 10 mmoles) dissolved in acetonitrile (80 ml). The mixture was heated under reflux for 30 mins. Evaporation of the solvent in vacuo gave colourless crystals (2 g, 52%) which were filtered off, and had m.p. 230-232° (from acetonitrile), λ_{max} 360 nm (shoulder) and 320 nm (ε 8456), ν_{max} 3260, 1650, 1570, 1320, 1230, 1100, 920, 780, 720 cm^{-1}, τ [($^2H_6$)DMSO], 1.0-1.05 (2H, α, m), 1.32-1.50 (1H, , m), 1.8-1.98 (2H, b, m), 2.36 (2H, β, s), 6.37 (4H, s).

(Found: C, 32.21; H, 3.56; N, 11.17 $C_{10}H_{13}Cl_2N_3O_8$ requires: C, 32.11; H, 3.48; N, 11.23%)

Attempted preparation of 6-N-picolyl-1H-1,4-diazepinium diperchlorate

Prepared by heating under reflux for 3 hrs a mixture of the pentadienium diperchlorate and ethylenediamine in ethanol, this salt had m.p. 240° (decomp.) (from acetonitrile), λ_{max} 328 and 263 nm (rough), ν_{max} 3300, 1660, 1630, 1580, 1320, 1100, 920, 810, 720 cm^{-1}, τ [($^2H_6$)DMSO] 1.06-1.13 (2H, d), 1.8 (2H, s), 1.92-1.98 (2H, d), 6.24 (4H, s), 7.33 (3H, s). (Found: C, 38.59; H, 4.09; N, 14.59 $C_{11}H_{15}Cl_2N_3O_8$ requires: C, 34.03; H, 3.89; N, 10.82%). The microanalysis result represents C:H:N ratio 12:16:4 .

One-pot reactions of the vinamidinium salts first with ammonia and then with the diamines to give the cyclised products

2,3-Dihydro-6-phenyl-1H-1,4-diazepinium perchlorate

Ammonia was bubbled steadily for 30 mins through a mixture of the pentadienium perchlorate (24), (1.36 g, 4.5 mmoles) in methanol (50 ml) which was heated under reflux. To the cooled mixture ethylenediamine (0.27 g, 4.5 mmoles) was added and the mixture was heated under reflux for a further 30 mins. Solvent was removed in vacuo and the crystalline product so formed was filtered off and washed with ether. This product (1 g, 85%) was identified, by its m.p. and mixed m.p. with the authentic compound.

1,4-Diethyl-2,3-dihydro-6-phenyl-1H-1,4-diazepinium perchlorate

Ammonia was passed through a refluxing solution of the pentadienium perchlorate (24), (3 g, 10 mmoles) in ethanol (100 ml) for 30 mins. N,N'-Diethylethylenediamine (1.2 g, 10 mmoles) was added to the cooled mixture which was then heated under reflux for 1 hr. Removal of the solvent in vacuo gave the product (2.5 g, 76%) which was filtered off and washed with ether. It had m.p. 68-70° (from ethanol), λ_{max} 369 and 253 nm (ε 11712 and 14283), ν_{max} 1630, 1560, 1150, 1080, 720 cm^{-1}, τ[($^2H_6$)DMSO], 1.93 (2H, s), 2.6 (5H, s). 5.9-6.4 (4H, q), 6.14 (4H, s), 8.54-8.77 (6H, t), (Found: C, 54.93; H, 6.55; N, 8.45 $C_{15}H_{21}ClN_2O_4$ requires: C, 54.80; H, 6.44; N, 8.52%)

2,3-Dihydro-5-methyl-6-phenyl-1H-1,4-diazepinium perchlorate

Ammonia was passed through a refluxing solution of the dianil vinamidinium perchlorate (78), (1.2 g, 3 mmoles) in methanol (80 ml) for 30 mins. The mixture was heated for another 15 mins, and the solution was then cooled and ethylenediamine (0.18 g, 3 mmoles) in methanol (20 ml) was added. The mixture was heated under reflux for 1 hr, and solvent was removed in vacuo giving a heavy surup which was kept at 0°C overnight. A colourless crystalline product (0.6 g, 73%) so formed was filtered off and washed with ether. It had m.p. 117-118° (from ethanol), λ_{max} 343 and 243 nm (ε 9707 and 7569), ν_{max} 3300, 1630, 1100, 720 cm^{-1}, τ [($^2H_6$)Acetone], 2.36 (1H, s), 2.62 (5H, m), 6.07 (4H, s), 7.94 (3H, s). (Found: C, 50.29; H, 5.31; N, 9.84 $C_{12}H_{15}ClN_2O_4$ requires: C, 50.27; H, 5.27; N, 9.77%)

2,3-Dihydro-1,5-dimethyl-6-phenyl-1H-1,4-diazepinium perchlorate

A solution of the corresponding dianil vinamidinium salt (4.1 g, 10 mmoles) in methanol (150 ml) was heated under reflux and ammonia was bubbled through this solution for 30 mins. N-Methylethylenediamine (0.74 g, 10 mmoles) in methanol (20 ml) was added to the cooled solution, which was again heated under reflux for 6 hrs. Removal of the solvent in vacuo gave an oil which gave a solid with difficulty after being kept at 0°C overnight followed by trituration with ether. The product (2.2 g, 67%) had m.p. 90° (from ethanol), λ_{max} 350 and 246 nm (ε 12699 and 5903), ν_{max} 3300, 1630, 1520, 1320, 1250, 1210, 1100, 980, 770, 710 cm^{-1}, τ[($^2H_6$)Acetone], 2.36 (1H, s), 2.64-2.80 (5H, b, m), 6.0-6.2 (4H, b, m), 6.40-6.60 (3H, m), 7.98 (3H, m). (Found: C, 51.80; H, 6.09; N, 9.63 $C_{13}H_{17}ClN_2O_4$ requires: C, 51.90; H, 5.71; N, 9.31%)

2,3-Dihydro-1,4,5-trimethyl-6-phenyl-1H-1,4-diazepinium perchlorate

This salt was prepared by first passing a stream of ammonia for 30 mins through a refluxing methanolic solution of the dianil salt (78) and then adding N,N'-dimethylethylenediamine and heating for a further 3 hrs. A crystalline product obtained on removal of the solvent in vacuo had m.p. 178-180° (from ethanol), λ_{max} 359 and 250 nm (ε 13989 and 7694), ν_{max} 1630, 1590, 1530, 1320, 1180, 1100, 770, 720, 700 cm^{-1}, τ [($^2H_6$)DMSO], 2.4 (1H, s), 2.6-2.80 (5H, b, m), 6.02-6.40 (4H, b, m), 6.62 (^{6}H, s), 7.94-8.0 (3H, m). (Found: C, 50.60; H, 6.15; N, 9.84 $C_{14}H_{19}ClN_2O_4$ requires: C, 53.42; H, 6.08; N, 8.90%). The analysis will be a fair representation if it is assumed that the product is contaminated

with (ca 10%) N,N'-dimethylethylenediamine perchlorate.

5-Benzyl-2,3-dihydro-6-methyl-1H-1,4-diazepinium perchlorate

A solution of the dianil vinamidinium salt (79), (2.1g, 10 mmoles) in ethanol (175 ml) was heated under reflux and ammonia was bubbled steadily through this refluxing solution for 30 min. The solution was cooled, and ethylenediamine (0.3 g, 5 mmoles) in ethanol (25 ml) was added to the solution which was heated under reflux for a further 4 hrs. The solvent was removed in vacuo, and the residue was kept at 0°C overnight in the presence of a little ether. The product (1.1 g, 75%) was filtered off and washed thoroughly with ether; it had m.p. 93-94°, λ_{max} 349 and 246 nm (shoulder) (ε 12992), ν_{max} 3300, 1300, 1060, 1040, 720 cm^{-1}, τ [TFA], 2.52-2.54 (1H, d), 2.6-2.82 (5H, m), 6.04 (2H, s), 6.26 (4H, m), 7.9 (3H, s). (Found: C, 51.23; H, 5.83; N, 9.37 $C_{13}H_{17}ClN_2O_4$ requires: C, 51.92; H, 5.70; N, 9.31%)

2,3-Dihydro-6-o-tolyl-1H-1,4-diazepinium perchlorate

Ammonia was passed through a mixture of the pentadienium perchlorate (61f) (2.7 g, 9 mmoles) in n-butanol (150 ml) which was heated under reflux for 30 min. Ethylenediamine (0.54 g, 9 mmoles) was added to the cooled solution and refluxing was continued for a further 1 hr. Removal of the solvent in vacuo gave a thick oil which crystallised very slowly at 0°C to a colourless crystalline product (1.9 g, 77%). This was filtered off and washed well with ether. It had m.p. 70° (from ethanolic perchloric acid), λ_{max} 347 and 238 nm (ε 9887 and 7217) ν_{max} 3300, 1630,

1225, 1100, 910, 720 cm^{-1}, τ [($^2H_6$)DMSO] 2.26-2.34 (2H, d), 2.55-2.80 (4H, m), 6.52 (4H, b), 7.75 (3H, s). (Found: C, 49.29; H, 5.41; N, 9.55 $C_{12}H_{15}ClN_2O_4$ requires: C, 50.29; H, 5.27; N, 9.77%)

2,3-Dihydro-2,2,3,3-tetramethyl-6-phenyl-1H-1,4-diazepinium perchlorate

A solution of the pentadienium salt (3 g, 10 mmoles) in n-butanol (150 ml) was heated under reflux and ammonia was passed through the solution for 30 mins. 2,3-Diamino-2,3-dimethylbutane (1.16 g, 10 mmoles) freshly prepared by reduction[20] of its dinitro compound was added and the mixture was heated for 4 hrs. The solvent was removed in vacuo, and when cooled the residue gave a solid. The product (2 g, 39%) with m.p. 145-146°, λ_{max} 350 and 245 nm (ε 5146 and 9292), ν_{max} 3280, 1630, 1520, 1100, 720 cm^{-1}, τ [($^2H_6$)DMSO] 2.25-2.34 (2H, d), 2.72 (5H, s), 8.61 (6H, s), 9.10 (6H, s). (Found: C, 54.17; H, 6.51; N, 8.28 $C_{15}H_{21}ClN_2O_4$ requires: C, 54.79; H, 6.34; N, 8.52%)

2,3-Dihydro-2,2,3,3-tetramethyl-1H-1,4-diazepinium perchlorate

This compound was prepared by heating under reflux for 3 hrs, a mixture of the corresponding dianil salt dissolved in n-butanol which had been saturated with ammonia gas, and 2,3-diamino-2,3-dimethylbutane. The product obtained after removing the solvent in vacuo had m.p. 80-85°, ν_{max} 3300, 1620, 1100, 720 cm^{-1}, τ [($^2H_6$)DMSO] 2.30-2.38 (2H, d), 4.58-4.74 (1H, t), 8.53 (6H, s), 9.06 (6H, s). No satisfactory analysis was obtained despite repeated attempts

of crystallisation.

Preparation of dihydrodiazepinium perchlorates using aryl-malondialdehyde salts

The following dihydrodiazepinium salts were prepared via aryl or p-substituted arylmalondialdehyde liberated in situ from its sodium salt prepared by the method of Eistert and Haupter [113]

2,3-Dihydro-1,4,6-triphenyl-1H-1,4-diazepinium perchlorate

Dianilinoethane (1.06 g, 5 mmoles) was added to phenyl-malondialdehyde liberated in situ by addition of perchloric acid (60%, 1 g, 10 mmoles) to a solution of the sodium salt phenyl-malondialdehyde (0.85 g, 5 mmoles) in methanol (10 ml). The yellow crystals, which had formed after 15 mins at room temperature, were filtered off after 30 min and finally washed with ether. The product (1.55 g, 59%) had m.p. 199-200° (from ethanol), λ_{max} 405 and 254 nm ($\mathcal{E}$ 22484 and 21482), ν_{max} 1620, 1580, 1520, 1270, 1080, 780 cm^{-1}, τ [($^2H_6$)DMSO], 1.7 (2H, s), 2.3-2.64 (15H, c, m), 5.4-5.6 (4H, b). (Found: C, 64.85; H, 4.84; N, 6.45 $C_{23}H_{21}ClN_2O_4$ requires: C, 64.97; H, 4.94; N, 6.59%)

2,3-Dihydro-1,6-diphenyl-1H-1,4-diazepinium perchlorate

This salt was prepared by adding N-phenylethylenediamine (0.14 g, 1 mmole), in methanol (2 ml) to a mixture of the sodium salt of phenylmalondialdehyde (0.17 g, 1 mmole) in methanol (5 ml) and perchloric acid (60%, 0.3 g, 3 mmoles), and then keeping the reaction mixture at room temperature overnight. The yellow product (0.11 g, 30%), which was obtained on addition of a little

ether, was filtered off. It had m.p. 158-160° (from ethanol), λ_{max} 376 and 245 nm (ε 15810 and 16782), ν_{max} 3300, 1630, 1530, 1300, 1250, 1100, 920, 780, 760, 700 cm^{-1}, τ [($^2H_6$)DMSO]+D_2O, 1.78-2.0 (2H, d), 2.43-2.55 (10H, m), 5.5-5.94 (4H, b). (Found: C, 58.36; H, 5.12; N, 7.75 $C_{17}H_{17}ClN_2O_4$ requires: C, 58.34; H, 4.87; N, 8.03%)

1,4-p-Dianisyl-2,3-dihydro-6-phenyl-1H-1,4-diazepinium perchlorate

Perchloric acid (60%, 0.42 g, 4 mmoles) was added to a mixture of the sodium salt of phenylmalondialdehyde (0.34 g, 2 mmoles) in methanol (25 ml), followed by N,N'-di-p-anisylethylenediamine (0.54 g, 2 mmoles). The yellow crystals which had formed after 3 hrs at room temperature were filtered off and finally washed with ether. The product (0.55 g, 58%) had m.p. 162-164° (from ethanol), λ_{max} 414 and 256 nm (ε 24246 and 16164), ν_{max} 1600, 1240, 1180, 1080, 1020, 830, 760, 720 cm^{-1}, τ [($^2H_6$)Acetone], 1.84 (2H, s), 2.38-2.46 (4H, d), 2.46-2.85 (5H, c, m), 2.89-2.98 (4H d), 5.30-5.50 (4H, b), 6.16 (6H, s). (Found: C, 61.25; H, 5.23; N, 5.73 $C_{25}H_{25}ClN_2O_6$ requires: C, 61.92; H, 5.20; N, 5.77%)

6-p-Anisyl-2,3-dihydro-1,4-diphenyl-1H-1,4-diazepinium perchlorate

Perchloric acid (0.2 g, 2 mmoles) was added to the sodium salt of p-anisylmalondialdehyde (0.2 g, 1 mmole) in methanol (3 ml), followed by dianilinoethane (0.2 g, 1 mmole). The mixture was stirred in an ice bath for 2 mins, and then at room temperature for another 15 mins, when perchloric acid (0.1 g, 1 mmole) was added. The uv spectrum indicated that cyclisation was complete after ca 20 mins. A little ice was added to the mixture and the

product (0.15 g, 33%) was filtered off and had m.p. 78°C, λ_{max} 414 and 253 nm (ε 16818 and 23297), ν_{max} 1610, 1240, 1180, 1100, 1020, 830, 760, 720 cm^{-1}, τ [($^2H_6$)Acetone], 1.78 (2H, s), 2.30-2.50 (10H, m), 2.5-2.54 (2H, d), 2.98-3.06 (2H, d), 5.2-5.34 (4H, b, m), 6.16 (3H, s). (Found: C, 63.70; H, 5.14; N, 6.78 $C_{24}H_{23}ClN_2O_5$ requires: C, 63.31; H, 5.06; N, 6.16%)

1,4-6-Tri-p-anisyl-2,3-dihydro-1H-1,4-diazepinium perchlorate

This salt, prepared by adding N,N'-di-p-anisylethylene-diamine to the p-anisylmalondialdehyde liberated from its sodium salt in methanol in situ by the addition of perchloric acid, had m.p. 70°, λ_{max} 424 and 259 and 229 nm (ε 20942 and 19053 and 18882), ν_{max} 1620, 1300, 1240, 1100, 1020, 830 cm^{-1}, τ [($^2H_6$)Acetone], 1.89 (2H, s), 2.38-2.47 (4H, d), 2.50-2.59 (2H, d), 2.88-2.98 (4H, d), 3.0-3.09 (2H, d), 5.34-5.48 (4H, b), 6.17 (9H, s). (Found: C, 60.66; H, 5.28; N, 5.19 $C_{26}H_{27}ClN_2O_7$ requires: C, 60.64; H, 5.24; N, 5.43%)

2,3-Dihydro-6-p-nitrophenyl-1,4-diphenyl-1H-1,4-diazepinium perchlorate

p-Nitrophenylmalondialdehyde was liberated from its sodium salt in methanol in situ by addition of perchloric acid. The dihydrodiazepinium salt was prepared by adding dianilinoethane dissolved in methanol to the free nitrophenylmalondialdehyde. It had m.p. 260° (from acetonitrile), λ_{max} 397, 275 (shoulder) and 235 nm (ε 22101 and 14270), ν_{max} 1630, 1590, 1500, 1310, 1100, 850, 760 cm^{-1}, τ [($^2H_6$)DMSO], 1.60 (2H, s), 1.72-1.80 (2H, d), 2.08-2.17 (2H, d), 2.32-2.48 (10H, c, m), 5.38-5.54 (4H, b).

(Found: C, 58.67; H, 4.26; N, 9.05 $C_{23}H_{20}ClN_3O_6$ requires: C: 58.79; H, 4.29; N, 8.94%)

2,3-Dihydro-6-p-nitrophenyl-1-phenyl-1H-1,4-diazepinium perchlorate

Perchloric acid (2 ml) was added to the sodium salt of p-nitrophenylmalondialdehyde (3.1 g, 15 mmoles) in methanol (200 ml), followed by N-phenylethylenediamine (1.3 g, 10 mmoles) in methanol (5 ml). The mixture was kept at room temperature overnight. The crystalline product (2.5 g, 44%) was filtered off and washed with ether. It had m.p. 196-197° (from acetonitrile), λ_{max} 374 and 230nm (ε 19548 and 14766), ν_{max} 3300, 1640, 1580, 1250, 1100, 1040, 930, 850, 720 cm^{-1}, τ [($^2H_6$)Acetone] 1.50 (1H, d), 1.64 (1H, d), 1.70-1.79 (2H, d), 2.14-2.22 (2H, d), 2.30-2.48 (5H, m), 5.32-5.44 (2H, b, m), 5.60-5.76 (2H, b, m). (Found: C, 51.71; H, 4.12; N, 10.86 $C_{17}H_{16}N_3ClO_6$ requires: C, 51.84; H, 4.09; N, 10.67%)

2,3-Dihydro-6-α-naphthyl-1,4-diphenyl-1H-1,4-diazepinium perchlorate

First, hydrolysis of α-naphthylpentadienium perchlorate with sodium hydroxide gave in situ the sodium salt of α-naphthylmalondialdehyde (this salt was not isolated because of its gel-like nature). Free α-naphthylmalondialdehyde was liberated from this salt by the addition of perchloric acid (3 times excess) in methanol and to this solution dianilinoethane was then added. A yellow crystalline product was obtained on keeping the mixture at room temperature for 5 mins. The product had m.p. 215-217°,

λ_{max} 403 and 292 (shoulder nm)(ε 23177), ν_{max} 1610, 1510, 1270, 1100, 930, 760 cm^{-1}, τ[($^2H_6$)DMSO], 1.82 (2H, s), 1.96-2.60 (7H, c, m), 2.4-2.46 (10H, m), 5.2-5.40 (4H, b, m). (Found: C, 68.02; H, 4.80; N, 5.81 $C_{27}H_{23}ClN_2O_4$ requires: C, 68.28; H, 4.88; N, 5.90%)

Preparation of 2, 3-dihydrodiazepinium salts using malondialdehyde tetraacetal

1,4-p-Dianisyl-2, 3-dihydro-1H-1, 4-diazepinium perchlorate

1, 1, 3, 3-Tetraethoxypropane (1 g) was dissolved in methanol (20 ml). N, N'-Di-p-anisylethylenediamine (1 g) was added, followed by a solution of perchloric acid (60%, 1.5 ml) in methanol (15 ml). The mixture was kept at room temperature overnight and the product (0.4 g, 30%) which had formed was filtered off and washed with ether, it had m.p. 167-168° (from ethanol), λ_{max} 390 nm (ε 25952), ν_{max} 1600, 1550, 1490, 1320, 1300, 1280, 1250, 1170, 1100, 1020, 820, 720 cm^{-1}, τ[($^2H_6$)DMSO], 1.9-1.98 (2H, d), 2.49-2.60 (4H, d), 2.84-2.94 (4H, d), 4.34-4.50 (1H, t), 5.50-5.84 (4H, b), 6.18 (6H, s). (Found: C, 55.85; H, 5.24; N, 6.77 $C_{19}H_{21}ClN_2O_6$ requires: C, 55.77; H, 5.14; N, 6.85%)

1,4-Di-p-chlorophenyl-2, 3-dihydro-1H-1, 4-diazepinium perchlorate

1, 1, 3, 3-Tetraethoxypropane (1.7 g) was dissolved in methanol (5 ml). N, N'-Di-p-chlorophenylethylenediamine (1.4 g) was added to this solution followed by perchloric acid (2 ml) in methanol (30 ml). The mixture was kept at room temperature for 24 hrs. Removal of the solvent in vacuo gave crystals (1.2 g, 43%) which had m.p. 162° (from ethanol), λ_{max} 360 nm (ε 11933), ν_{max} 1620, 1590, 1540,

1330, 1285, 1200, 1100, 1000, 950, 820, 750 cm^{-1}, τ[($^2H_6$)DMSO] 1.79-1.87 (2H, d), 2.4-2.42 (8H, d), 4.26-4.42 (1H, t), 5.48-5.66 (4H, b). (Found: C, 48.11; H, 3.60; N, 5.82 $C_{17}H_{15}Cl_3N_2O_4$ requires: C, 48.89; H, 3.62; N, 5.71%)

2,3-Dihydro-1,4-p-ditolyl-1H-1,4-diazepinium perchlorate

N,N'-Di-p-tolylethylenediamine (2.4 g) was added to a solution of 1,1,3,3-tetraethoxypropane (2.4 g) in methanol (5 ml), followed by perchloric acid (4 ml) in methanol (50 ml). The mixture was warmed in a water bath (60°C) for 5 mins, and then kept at room temperature overnight. Removal of the solvent in vacuo yielded the product (1.8 g, 55%) which had m.p. 158-160° (from ethanol), λ_{max} 384 nm (ε 27172), ν_{max} 1510, 1300, 1100, 1000, 880, 810, 720 cm^{-1}, τ[TFA], 2.14-2.22 (2H, d), 2.56-2.64 (4H, d), 2.72-2.80 (4H, d), 4.22-4.39 (1H, t), 5.42-5.80 (4H, b), 7.57 (6H, s). (Found: C, 59.70; H, 5.61; N, 7.10 $C_{19}H_{21}ClN_2O_4$ requires: C, 60.50; H, 5.57; N, 7.43%)

Preparation of 2,3-dihydro-1,4-diazepinium perchlorates from β-diketones

2,3-Dihydro-2,2,3,3,5,7-hexamethyl-1H-1,4-diazepinium perchlorate

Acetylacetone (0.2 g, 2 mmoles) was added to 2,3-diamino-2,3-dimethylbutane (0.23 g, 2 mmoles) in glacial acetic acid (1 ml). The mixture was warmed in a flask fitted with a drying tube in a water bath maintained at 80-85°C for 8 hrs. Perchloric acid (60%, 0.3 g) was added to the cooled solution, and the crystalline solid obtained was filtered off and washed with ether. The product (0.3 g, 54%) had

m.p. 253-254° (from ethanol), λ_{max} 319 nm (ε 14685), ν_{max} 3290, 1590, 1150, 1100, 780 cm^{-1}, τ [($^2H_6$)Acetone], 0.9-1.4 (NH, b), 4·69-4·74 (1H, t), 7.68 (6H, s), 8.51 (6H, s), 8.94 (6H, s). (Found: C, 47.09; H, 6.88; N, 10.38 $C_{11}H_{21}ClN_2O_4$ requires: C, 47.06; H, 7.53; N, 9.97%)

5,7-Diethyl-2,3-dihydro-2,2,3,3-tetramethyl-1H-1,4-diazepinium perchlorate

3,5-Heptanedione (0.64 g, 5 mmoles) and 1,2-diamino-1,2-dimethylbutane (0.58 g, 5mmoles) in acetic acid (2 ml) were heated under reflux for 40 hrs. To the cooled mixture perchloric acid (60%, 0.5 g) was added, and the crystalline product (0.55 g, 36%) was filtered off and washed with ether, it had m.p. 130° (from ethanol), λ_{max} 322 nm (ε 9140), ν_{max} 3300, 1600, 1520, 1250, 1100, 1050, 920, 820 cm^{-1}, τ[($^2H_6$)DMSO], 0.42-0.60 (NH, b), 4.80-4.84 (1H, t), 7.46-7.69 (4H, q), 8.66 (6H, s), 8.76-8.92 (6H, t), 9.14 (6H, s). (Found: C, 50.50; H, 7.81; N, 9.10 $C_{13}H_{25}ClN_2O_4$ requires: C, 50.56; H, 8.16; N, 9.07%)

Preparation of 6-bromo-2,3-dihydro-1H-1,4-diazepinium perchlorate via the dianil salt prepared by decarboxylation of mucobromic acid

Aniline (1.86 g, 20 mmoles) dissolved in ethanol (20 ml) was slowly added to a cooled stirred solution of mucobromic acid (2.6 g, 10 mmoles) in ethanol (30 ml). The mixture was stirred for 30 mins at room temperature, concentrated by removal of the solvent in vacuo, cooled and ether was added. The solid (1.9 g) was filtered off; it had m.p. 216-219°.

To the dianil bromide (1.7 g, 5 mmoles) dissolved in ethanol (80 ml), ethylenediamine (0.3 g, 5 mmoles), in ethanol (20 ml) was added in one portion and the mixture was heated under reflux for 2 hrs. Removal of the solvent in vacuo gave the solid which was filtered off and washed with ether, it had m p. 155° (from ethanolic perchloric acid, lit. m.p. 154-155°). The product was also identified by its mixed m.p. with the authentic compound.

Preparation of 2, 3-dihydro-5-methoxy-7-phenyl-1H-1, 4-diazepinium fluoroborate from 7-phenyl-1, 2, 3, 4-tetrahydro-1, 4-diazepine-5-one

The keto compound (0.37 g, 2 mmoles), prepared as described by Hofman and Safir[170], was dissolved in dried methylene chloride (20 ml). Trimethyloxoniumfluoroborate (0.3 g, 2 mmoles) was added to the solution which was kept at room temperature overnight. The solvent was concentrated in vacuo, and ether was added to the cooled solution. The colourless crystals produced were filtered off and washed with ether. The product (0.4 g, 70%) had m.p. 130-132° (from ethanol), λ_{max} 320 and 245 nm (ε 15890 and 9080), ν_{max} 3320, 1620, 1320, 1250, 1235, 1165, 1100, 850, 790, 700 cm^{-1}, τ [TFA] 2.32-2.48 (5H, m), 4.7-4.8 (1H, b), 5.92 (3H, s), 6.0-6.2 (4H, b, m). (Found: C, 49.77; H, 5.25; N, 9.40 $C_{12}H_{15}BF_4N_2O$ requires: C, 49.69; H, 5.21; N, 9.60%)

Electrophilic Substitution of dihydrodiazepinium Salts

(a) Halogenation

(i) Using elemental bromine

6-p-Bromophenyl-2,3-dihydro-1H-1,4-diazepinium perchlorate

Bromine (0.64 g, 4 mmoles) in methanol (10 ml) was added dropwise to a stirred solution of the corresponding unsubstituted phenyldiazepinium salt (1 g, 4 mmoles) in methanol (40 ml) at room temperature. The mixture was stirred for two hours and then addition of ether provided the 6-p-bromophenyl compound (0.6 g, 65%) which had m.p. 285-287° (from ethanolic perchloric acid), λ_{max} 352 and 254 nm (ε 7816 and 16510), ν_{max} 3300, 1640, 1540, 1310, 1100, 1040, 920, 820, 720 cm^{-1}, τ [($^2H_6$)DMSO], 2.04-2.12 (2H, m), 2.42-2.51 (2H d), 2.66-2.77 (2H, d), 6.23 (4H, s). (Found: C, 37.52; H 3.41; N, 7.91 $C_{11}H_{12}BrClN_2O_4$ requires: C, 37.56; H, 3.44; N, 7.96%)

6-p-Bromophenyl-2,3-dihydro-1,4-dimethyl-1H-1,4-diazepinium perchlorate

Prepared from the corresponding unsubstituted phenyldiazepinium salt (0.6 g, 2 mmoles) and bromine (0.32 g, 2 mmoles), this salt (0.35 g, 40% had m p. 180° (from ethanolic perchloric acid), λ_{max} 366 and 262 nm (ε13430 and 19400), ν_{max} 1640, 1580, 1320, 1240, 1100, 950, 830, 720 cm^{-1}, τ [($^2H_6$)DMSO], 2.02 (2H, s), 2.39-2.47 (2H, d), 2.65-2.76 (2H, d), 6.2 (4H, s), 6.67 (6H, s). (Found: C, 40.87; H, 4.34; N 7.28 $C_{13}H_{16}BrClN_2O_4$ requires: C, 41.09; H 4.22; N, 7.38%).

6-p-Bromophenyl-2,3-dihydro-1-methyl-1H-1,4-diazepinium perchlorate

To a stirred methanolic solution of the corresponding

unsubstituted phenyldiazepinium salt (2.8 g, 10 mmoles), bromine (1.6 g, 10 mmoles) was added dropwise and the mixture was stirred for 4 hrs.at room temperature. Removal of this solvent in vacuo gave the product (1.2 g, 53%) which had m.p. 184-186° (from ethanolic perchloric acid), λ_{max} 360 and 258 nm (ε 9663 and 151810), ν_{max} 3300, 1640, 1560, 1330, 1240, 1170, 1100, 930, 820 cm^{-1}, τ [($^2H_6$)DMSO], 1.93 (1H, s), 2.01-2.10 (1H, d), 2.37-2.45 (2H, d), 2.64-2.72 (2H, d), 6.2 (4H, s), 6.47 (3H, s). (Found: C, 39.62; H, 3.63; N, 7.58 $C_{12}H_{14}BrClN_2O_4$ requires: C, 39.42; H, 3.86; N, 7.66%)

6-p-Bromophenyl-2,3-dihydro-2-methyl-1H-1,4-diazepinium perchlorate

Prepared from the corresponding unsubstituted phenyldiazepinium salt (1.7 g, 6 mmoles) and bromine (6 mmoles), this compound (0.85 g, 40%) had m.p. 228-231° (from ethanolic perchloric acid), λ_{max} 354 and 255 nm (ε 8435 and 16720), ν_{max} 3300, 1540, 1540, 1320, 1100, 820, 730 cm^{-1}, τ [($^2H_6$)DMSO)] [-0.4-(-0.8) (2H, b)], 1.94-2.02 (1H, d), 2.07-2.16 (1H, d), 2.37-2.44 (2H, d), 2.64-2.73 (2H, d), 5.80-6.2 (1H, b), 6.34-6.50 (2H, m), 8.73-8.80 (3H, d). (Found: C, 39.51; H, 3.92; N, 7.74 $C_{12}H_{14}BrClN_2O_4$ requires: C, 39.42; H, 3.86; N, 7.66%)

6-p-Bromophenyl-2,3-dihydro-2,2-dimethyl-1H-1,4-diazepinium perchlorate

Prepared from the corresponding unsubstituted phenyldiazepinium salt (1.2 g, 4 mmoles) and bromine (0.64 g, 4 mmoles), this salt (0.5 g, 33%) had m.p. 214° (decomp.), λ_{max} 352 and 254 nm (ε 8210 and 16580), ν_{max} 3300, 1640, 1530,1320, 1100, 820,

730 cm^{-1}, τ[($^2H_6$)DMSO] 1.86 (1H, d), 2.26 (1H, d), 2.37-2.46 (2H, d), 2.62-2.72 (2H, d), 6.50-6.80 (2H, b), 8.70 (6H, s). (Found: C, 41.52; H, 3.52; N, 7.85 $C_{13}H_{14}BrClN_2O_4$ requires: C, 41.31; H, 3.71; N, 7.42%)

6-p-Bromophenyl-2,3-cyclohexano-2,3-dihydro-1H-1,4-diazepinium perchlorate

Bromine (0.18 g, 1 mmoles) in methanol (10 ml) was added dropwise to a stirred solution of the corresponding unsubstituted 6-phenyldiazepinium perchlorate (0.3 g, 1 mmoles) in methanol (5 ml). The mixture was stirred for ca 5 hours and removal of the solvent in vacuo provided a crystalline product (0.12 g, 32%) which was filtered off and washed with ether; it had m.p. 278-280° (from ethanolic perchloric acid), λ_{max} 356 and 256 nm (ε 7709 and 17850) ν_{max} 3300, 1540, 1540, 1330, 1100, 820, 720 cm^{-1} τ[($^2H_6$)DMSO] 2.22 (2H, s), 2.33-2.47 (2H, d), 2.6-2.77 (2H, d), 6.6-6.88 (2H, b), 8.1-8.7 (8H, c, m, b). (Found: C, 44.89; H, 4.79; N, 7.10 $C_{15}H_{18}BrClN_2O_4$ requires: C, 44.37; H, 4.74; N, 6.90%)

Attempted preparation of 6-p-bromophenyl-2,3-dihydro-1,4-diphenyl-1H-1,4-diazepinium perchlorate

A solution of the corresponding unsubstituted 1,4,6-triphenyldiazepinium perchlorate (0.43 g, 1 mmoles) and bromine (0.16 g, 1 mmole) in methanol was kept for nearly 5 days at room temperature. The solid (0.4 g) obtained by precipitation with ether had identical uv, melting point and mixed melting point to the starting material.

Similarly, the attempted bromination of 1,4-dibenzyl-1,3-dihydro-1H-1,4-diazepinium perchlorate in methanol at room temperature after ca 24 hrs resulted only in the recovery of the starting material.

Attempted bromination of 2,3-dihydro-6-p-methoxyphenyl and also of 6-p-methylphenyl-1H-1,4-diazepinium perchlorates

These salts were not brominated in methanolic solution, and in each case the starting material was recovered in quantitative yield.

6-p-Bromophenyl-1,4-diethyl-2,3-dihydro-1H-1,4-diazepinium perchlorate

Bromine (1.6 g, 10 mmoles) in methanol (20 ml) was added dropwise to a stirred solution of the corresponding unsubstituted 6-phenyldiazepinium salt (3 g, 10 mmoles) in methanol (20 ml). The mixture was stirred for a further five hours at room temperature and then the solvent was removed in vacuo. This gave the product (2.6 g, 70%) which had m.p. 64° (from ethanolic perchloric acid), λ_{max} 368 and 263 nm (ε 13438 and 21441), ν_{max} 1610, 1300, 1240, 1100, 820, 720 cm^{-1}, τ [(TFA], 2.26 (2H, s), 2.44-2.53 (2H, d), 2.82-2.90 (2H, d), 6.06 (4H, s), 6.10-6.32 (4H, q) 8.49-8.64 (6H, t). (Found: C, 44.67; H, 5.08; N, 7.02 $C_{15}H_{20}BrClN_2O_4$ requires: C, 44.19; H, 4.95; N, 6.87%).

1,4-Di-p-anisyl-6-p-bromophenyl-2,3-dihydro-1H-1,4-diazepinium perchlorate

Prepared from the corresponding unsubstituted 6-phenyldiazepinium salt (0.48 g, 1 mmole) in methanol (10 ml) and bromine

(0.15 g, 1 mmole) in methanol (5 ml), this salt (0.35 g, 62%) had m.p. 128-130° (from ethanolic perchloric acid), λ_{max} 414, 256 and 223 nm (ε 24808 and 16895 and 18606), ν_{max} 1740, 1600, 1580, 1300, 1240, 1160, 1100, 1020, 820, 720, 690 cm^{-1}, τ[($^2H_6$)acetone] 1.87 (2H, s), 2.25-2.34 (4H, d), 2.38-2.66 (4H, m), 2.87-2.96 (4H, d), 5.28 (4H, m), 6.15 (6H, s). (Found: C, 53.78; H, 4.16; N, 4.22 $C_{25}H_{24}BrClN_2O_6$ requires: C, 53.26; H, 4.29; N, 4.97%)

Attempted bromination of 2,3-dihydro-2,2,3,3-tetramethyl-6-phenyl-1H-1,4-diazepinium perchlorate

When an equivalent amount of bromine was used, it gave a product which from its analysis appeared to be only partially brominated. (Found: C, 46.17; H, 5.56; N, 7.61 $C_{15}H_{20}BrClN_2O_4$ requires: C, 44.21; H, 4.91; N, 6.87%).

6-Bromo-α-naphthyl-2,3-dihydro-1H-1,4-diazepinium perchlorate

To a stirred methanolic solution of the corresponding unsubstituted α-naphthyldiazepinium salt (1.6 g, 5 mmoles) bromine (0.8 g, 5 mmoles) in methanol (10 ml) was added dropwise after a period of ca 20 minutes, and the mixture was stirred for a further six hours. The solvent was removed in vacuo. This gave crystals which were filtered off and washed with ether. The product (1.3 g, 67%) had m.p. 198-200° (from ethanolic perchloric acid), λ_{max} 348 and 323 (shoulder) and 301 nm (ε 8033 and 9790), ν_{max} 3300, 1640, 1540, 1310, 1240, 1100, 950, 920, 820, 760, 720 cm^{-1}, τ[($^2H_6$)DMSO] 2.01 (2H, s), 2.09-2.65 (6H, c, m), 6.12 (4H, m). (Found: C, 44.94; H, 3.87; N, 6.77 $C_{15}H_{14}BrClN_2O_4$ requires: C, 44.86; H, 3.51; N, 6.97%)

6-Bromo-β-naphthyl-2,3-dihydro-1H-1,4-diazepinium perchlorate

The product obtained when a methanolic solution of the corresponding unsubstituted β-naphthyldiazepinium salt was stirred with bromine had m.p. 223-224° (from ethanolic perchloric acid), λ_{max} 348, 324 (shoulder), 285 (shoulder) and 256 nm (ε 10623 and 21507), ν_{max} 3300, 1640, 1550, 1300, 1240, 1100, 950, 820, 760, 720 cm^{-1}, τ [($^2H_6$)DMSO] 1.68 (1H,d), 1.77 (1H,d), 1.84-2.50 (6H,c,m), 6.14 (4H,m). (Found: C, 45.31; H, 3.71; N, 6.99 $C_{15}H_{14}BrClN_2O_4$ requires: C, 44.86; H, 3.51; N 6.98%)

Bromination of the following compounds was also attempted but only the starting material was recovered in each case: 1,4-Dibenzyl-2,3-dihydro-6-α-naphthyl-1H-1,4-diazepinium perchlorate; 1,4-Dibenzyl-2,3-dihydro-6-β-naphthyl-1H-1,4-diazepinium perchlorate; 2,3-Dihydro-6-p-biphenyl-1H-1,4-diazepinium perchlorate; 2,3-Dihydro-5-methyl-6-phenyl-1H-1,4-diazepininium perchlorate; 5-Benzyl-2,3-dihydro-6-methyl-1H-1,4-diazepinium perchlorate; 2,3-Dihydro-6-o-tolyl-1H-1,4-diazepinium perchlorate; 2,3-Dihydro-6-N-pyridyl-1H-1,4-diazepinium perchlorate; 2,3-Dihydro-5-methoxy-7-phenyl-1H-1,4-diazepinium fluoroborate; 2,3-Dihydro-1,6-diphenyl-1H-1,4-diazepinium perchlorate; and 5,7-Diethyl-2,3-dihydro-2,2,3,3-tetramethyl-1H-1,4-diazepinium perchlorate.

6-Bromo-2,3-dihydro-1,4-di-p-methoxyphenyl-1H-1,4-diazepinium perchlorate

Bromine (0.16 g, 1 mmole) in methanol (4 ml) was added dropwise to the stirred solution of the corresponding unsubstituted

diazepinium salt (0.4 g, 1mmole). The mixture was stirred for 0.5 hr, the solvent remained in vacuo, and the product (0.28 g, 87%) was filtered off. It had m.p. 204-206° (from ethanolic perchloric acid), λ_{max} 419, 280 (shoulder) and 288 nm (ε 27567 and 17176), ν_{max} 1600, 1500, 1300, 1250, 1170, 1100, 1020, 820, 720 cm^{-1}, τ [TFA] 2.18-2.25 (2H, s), 2.61-2.70 (4H, d), 2.85-2.94 (4H, d), 5.50-5.80 (4H, b), 6.06 (6H, s). (Found: C, 46.62; H, 4.21; N, 6.01 $C_{19}H_{20}BrClN_2O_6$ requires: C, 46.79; H, 4.13; N, 5.74%)

6-Bromo-2,3-dihydro-5-methyl-1H-1,4-diazepinium picrate

Prepared from the corresponding unsubstituted diazepinium picrate and bromine in methanol, this salt had m.p. 278-280° λ_{max} 354 nm (ε 20396), ν_{max} 3500, 1600, 1540, 1270, 1150, 930, 900, 720 cm^{-1}, τ [($^2H_4$)MeOH] 1.04 (1H, s), 6.71 (4H, m), 7.47 (3H, s). (Found: C, 29.70; H, 2.82; N, 5.81 $C_{12}H_{12}Br_4N_2$ requires: C, 30.00; H, 2.52; N, 5.84%)

6-Bromo-2,3-dihydro-2,2,3,3,5,7-hexamethyl-1H-1,4-diazepinium perchlorate

Prepared from the corresponding unsubstituted diazepinium perchlorate and bromine in methanol, this salt (70%) had m.p. 155-160° (from ethanolic perchloric acid) λ_{max} 343 and 328 nm (ε 9077 and 8906), ν_{max} 3300, 1590, 1130, 1080, 770 cm^{-1}, τ[($^2H_6$)Acetone] 7.69 (6H, s), 8.52 (6H, s), 8.95 (6H, s). (Found: C, 36.87; H, 6.07; N, 8.27 $C_{11}H_{20}BrClN_2O_4$ requires: C, 36.74; H, 5.61; N, 7.79%)

(ii) Using N-halosuccinimides

6-p-Bromophenyl-2,3-dihydro-1H-1,4-diazepinium perchlorate

N-Bromosuccinimide (0.44 g, 2.5 mmoles) was added to the corresponding unsubstituted phenyldiazepinium perchlorate (0.68 g, 2.5 mmoles) in acetic acid (15 ml). The mixture was heated under reflux for 15 mins and then cooled. The product was filtered off and washed with a little water. The product (0.32 g, 37%) had m.p. 286°(from ethanolic perchloric acid). It was identified by its mixed m.p. with the genuine sample

6-p-Bromophenyl-2,3-dihydro-2-methyl-1H-1,4-diazepinium perchlorate

A solution of the corresponding unsubstituted phenyldiazepinium perchlorate (2.3 g) in acetic acid (20 ml) was added to N-bromosuccinimide (1.4 g) and the mixture was heated under reflux for 3 hrs. A crystalline product formed when the contents of the flasks were cooled. The crystals were filtered off and washed with water. The product (0.9 g, 31%) had an identical m.p. and mixed m.p. with that of the genuine sample

6-p-Bromophenyl-2,3-dihydro-1-methyl-1H-1,4-diazepinium perchlorate

Prepared from the corresponding unsubstituted phenyldiazepinium perchlorate and N-bromosuccinimide in acetic acid, this salt, after recrystallisation from ethanolic perchloric acid, had the same m.p. and mixed m.p. as that of the genuine sample

6-p-Bromophenyl-2,3-dihydro-1,4-dimethyl-1H-1,4-diazepinium perchlorate

This salt (0.6 g, 53%) prepared by heating a solution of the corresponding unsubstituted diazepinium perchlorate (0.9 g, 3 mmoles) and N-bromosuccinimide (0.53 g, 3 mmoles) in acetic acid (10 ml) under reflux for 3.5 hrs, had the identical m.p., mixed m.p. and uv to that of the genuine sample

Attempted bromination of the following compounds using N-bromosuccinimide gave only the starting material in quantitative yield in each case:

2,3-Dihydro-2,2-dimethyl-6-phenyl-1H-1,4-diazepinium perchlorate; 2,3-Cyclohexano-2,3-dihydro-6-phenyl-1H-1,4-diazepinium perchlorate; 1,4-Dibenzyl-2,3-dihydro-6-phenyl-1H-1,4-diazepinium perchlorate.

2,3-Dihydro-6-p-iodophenyl-1H-1,4-diazepinium perchlorate

N-Iodosuccinimide (1.1 g, 5 mmoles) was added to the corresponding unsubstituted phenyldiazepinium perchlorate (1.3 g, 5 mmoles) in acetic acid (25 ml). The mixture was heated under reflux for 15 mins and the cooled reaction mixture gave crystals which were filtered off and washed with ether. The product (1.5 g, 79%) had m.p. 298° (from ethanolic perchloric acid), λ_{max} 356 and 295 nm (ε 8291 and 19132), ν_{max} 3300, 1640, 1540, 1310, 1220, 1100, 1040, 820, 720 cm^{-1}, τ [($^2H_6$)DMSO] (-0.21-(-0.5)$_{broad}^{NH}$) 2.04 (2H, s), 2.22-2.31 (2H, d), 2.80-2.88 (2H, d), 6.27 (4H, s). (Found: C, 33.25; H, 2.97; N, 7.00. $C_{11}H_{13}ClIN_2O_4$ requires: C, 33.18; H, 3.01; N, 7.03%)

2,3-Dihydro-6-p-iodophenyl-2-methyl-1H-1,4-diazepinium perchlorate

A mixture of the corresponding unsubstituted phenyldiazepinium perchlorate (1.43 g, 5 mmoles) and N-iodosuccinimide (1.1 g, 5 mmoles) in acetic acid (25 ml) was heated under reflux for 2.5 hrs, cooled, and the product was filtered off and washed with a little ether. The product (1.4 g, 68%) had m.p. 270-272° (from ethanolic perchloric acid, λ_{max} 356 and 259 nm (ε 8405 and 21089), ν_{max} 3300, 1540, 1550, 1330, 1100, 1040, 960, 950, 920, 820, 790, 730 cm^{-1}, τ [($^2H_6$)DMSO] -0.3-(-0.54) (NH, b), 2.01 (1H, d), 2.14 (1H, d), 2.23-2.31 (2H, d), 2.80-2.90 (2H, d), 5.06-6.14 (1H, b, m), 6.42-6.46 (2H, m), 8.75-8.81 (3H, d). (Found: C, 35.06; H, 3.50; N, 6.84 $C_{12}H_{14}ClIN_2O_4$ requires: C, 34.90; H, 3.39; N, 6.79%)

2,3-Dihydro-6-p-iodophenyl-2,2-dimethyl-1H-1,4-diazepinium perchlorate

This salt (0.5 g, 39%), prepared by heating a solution of the corresponding unsubstituted phenyldiazepinium perchlorate (1.2 g, 4 mmoles) and N-iodosuccinimide (0.9 g, 4 mmoles) in acetic acid (15 ml) under reflux for 6 hrs, had m.p. 234-237° (from ethanolic perchloric acid), λ_{max} 352 and 259 nm (ε 8533 and 23323), ν_{max} 3280, 1640, 1530, 1320, 1100, 820, 720 cm^{-1}, τ [($^2H_6$)DMSO] 2.0 (1H, d), 2.20-2.33 (2H, d), 2.30 (1H, d), 2.77-2.90 (2H, d), 6.46-6.60 (2H, b), 8.7 (6H, s). (Found: C, 36.75; H, 3.69; N, 6.57 $C_{13}H_{16}ClIN_2O_4$ requires: C, 36.57; H, 3.75; N, 6.56%)

Each of the following compounds was recovered unchanged when heated with N-iodosuccinimide in glacial acetic acid:

1,4-Dibenzyl-2,3-dihydro-6-phenyl-1H-1,4-diazepinium perchlorate; 2,3-Dihydro-1,4-dimethyl-6-phenyl-1H-1,4-diazepinium perchlorate; 2,3-Cyclohexano-2,3-dihydro-6-phenyl-1H-1,4-diazepinium perchlorate; 2,3-Dihydro-1-methyl-6-phenyl-1H-1,4-diazepinium perchlorate; and 2,3-Dihydro-5-methoxy-7-phenyl-1H-1,4-diazepinium perchlorate.

Attempted chlorination of the 2,3-dihydro-6-phenyl-1H-1,4-diazepinium perchlorate and of 2,3-dihydro-2-methyl-6-phenyl-1H-1,4-diazepinium perchlorate using N-chlorosuccinimide also gave only the starting material in quantitative yield in each case.

6-Bromo-2,3-dihydro-5-methoxy-7-phenyl-1H-1,4-diazepinium perchlorate

N-Bromosuccinimide (0.53 g, 3 mmoles) was added to the corresponding unsubstituted diazepinium perchlorate (0.84 g, 3 mmoles) in acetic acid (15 ml) and the mixture was heated under reflux for 1 hr. It was cooled, and the product (0.6 g, 56%) was filtered off and washed with ether; it had m.p. 192°, λ_{max} 335 and 260 nm (shoulder) (ε 11352) ν_{max} 3320, 1590, 1310, 1260, 1210, 1050, 1080, 850, 765, 720, 690 cm^{-1}, τ [($^2H_6$)Acetone] 1.2-1.4 (NH, b), 2.52 (5H, s), 5.72 (3H, s), 6.05 (4H, s). (Found: C, 39.05; H, 3.86; N, 7.67 $C_{12}H_{24}BBrF_4N_2O$ requires: C, 39.06; H, 3.83; N, 7.59%)

Attempted oxidation reaction of 6-bromo-α-naphthyl-2,3-dihydro-1H-1,4-diazepinium perchlorate with potassium permanganate

The bromodiazepinium salt (0.4 g, 1 mmole) was added to water (5 ml) and conc. hydrochloric acid (5 ml). The mixture was warmed for 0.5 hr with potassium permanganate (0.5 g), cooled, and sulphur dioxide was passed through the mixture which was

extracted with ether. The organic layer was dried over anhydrous sodium sulphate, and the solvent was removed in vacuo. The product obtained could not be identified.

When the experiment was repeated with 6-bromo-β-naphthyl-diazepinium salt, a similar result was obtained. Only polymeric product was obtained.

(b) Nitration

2,3-Dihydro-1H-6-p-nitrophenyl-1,4-diazepinium nitrate

The corresponding unsubstituted phenyldiazepinium perchlorate (6 g) was added in small portions to stirred ice-cold nitric acid (60 ml nitric acid and 12 ml water). The mixture was stirred at room temperature for 2.5 hrs, and the brown solution was then poured into stirred water (215 ml), cooled in a solid carbon dioxide/acetone mixture. The nitro compound (2.8 g, 58%) which was filtered off had m.p. 240° (from methanol), λ_{max} 344nm (ε 17410), ν_{max} 3240, 1650, 1590, 1510, 1310, 1110, 1030, 920, 870, 800, 750, 700 cm^{-1}, τ [($^2H_6$)DMSO] 1.78-1.87 (2H, d), 1.74-1.83 (2H, d), 2.33-2.42 (2H, d). 6.18 (4H, m). (Found: C, 46.89; H, 4.19; N, 19.82 $C_{11}H_{12}N_4O_5$ requires: C, 47.14; H, 4.31; N, 19.99%)

Attempted preparation of a 2,3-dihydro-1,4-dimethyl-6-p-nitrophenyl-1H-1,4-diazepinium salt

Treatment of the corresponding unsubstituted phenyldiazepinium perchlorate (1.5 g) with nitric acid (15 ml) in water (3 ml) gave a solid (0.17 g, 22%) which was identified as p-nitrobenzoic acid by its

mass spectrum, ^{1}H nmr spectrum, m.p. 238-240° (from nitrmethane) and mixed m. p. 236-241° with the authentic compound (240-241°).

Attempted nitration of the 2, 3-dihydro-1-methyl-1H-1,4-diazepinium perchlorate also gave p-nitrobenzoic acid as did attempted nitration of 2, 3-dihydro-2-methyl-1H-1, 4-diazepinium perchlorate.

Reduction of nitro derivative and diazotisation of product.

6-p-Aminophenyl-2, 3-dihydro-1H-1, 4-diazepinium nitrate

The corresponding p-nitrophenyl diazepinium nitrate (1.5 g) was dissolved in ethanol (20 ml) by warming the solution to ca 60°. Palladium-charcoal (0.05 g) previously moistened with a little ethanol was added to the stirred solution, followed by hydrazine hydrate (1.5 g) and the mixture was heated under reflux for ca 2 hrs. The catalyst was removed by gentle filtration, and the filtrate was concentrated in vacuo and finally brought to boiling over a steam bath. Hot water (20 ml) was added slowly, and the mixture was then allowed to cool, and the product was filtered off. The m.p. of the crude product (0.6 g, 51%) was found to be 186-192°; it had λ_{max} 325 and 270 nm with the corresponding bathochromic shifts to 300 and 240 nm with dil. H_2SO_4.

The amino-compound was identified by its mass spectrum (m/e 188) and by the mass spectrum of its acetylated compound (m/e 229) prepared by the addition of acetic anhydride.

Attempted repetitions of this reduction failed to provide the amino compound.

Attempted diazotisation of the 2,3-dihydro-6-p-aminophenyl-1H-1,4-diazepinium salt

The 6-aminophenyl salt (0.16 g) was added to cold stirred fluoroboric acid (10 ml) followed by slow addition of cold sodium nitrite solution (0.07 g). A solid product (0.08 g, 48%) had melting point (crude) 174-177° and mixed melting point 155-160° with the corresponding amino-compound.

Attempted diazo-coupling of the 2,3-dihydro-6-phenyl-1H-1,4-diazepinium perchlorate with p-nitrophenyldiazonium chloride

The diazepinium perchlorate in methanol was added to p-nitrophenyldiazonium chloride, and the mixture was stirred for 1 hr at room temperature. The coloured solid obtained had m.p. 110-116° (decomp.), but could not be identified. Attempts to recrystallise it from ethanol resulted in evolution of a gas (probably nitrogen) and gave a very dark solution.

(C) Acylation

(i) Attempted formylation of 2,3-dihydro-6-phenyl-1H-1,4-diazepinium perchlorate using Vilsmeier formylating reagent

Phosphoryl chloride (1.53 g, 10 mmoles) was added slowly to cold stirred dimethylformamide (20 ml) followed by the corresponding unsubstituted diazepinium perchlorate (2.18 g, 8 mmoles) in dimethylformamide (20 ml). The mixture was stirred for 1 hr and kept overnight at room temperature and finally poured into 0.33 M aqueous sodium hydroxide (300 ml).

The mixture was extracted with ether and the etheral layer was dried over anhydrous sodium sulphate. The inorganic sulphate was filtered off and to the filtrate freshly prepared 2,4-dinitrophenylhydrazine (2 g) was added. The analysis of the final product by its ^{1}H nmr spectrum showed it to be the unchanged 2,4-dinitrophenylhydrazine.

(ii) Acetylation: Attempted acetylation of 2,3-dihydro-6-phenyl-1H-1,4-diazepinium perchlorate using acetic anhydride

Phenyldiazepinium perchlorate (0.5 g) was dissolved in excess of acetic anhydride (10 ml) and a small amount of glacial acetic acid was added. The mixture was kept at room temperature for ca 6 days but unchanged starting material was recovered quantitatively.

(iii) Methylation

2,3-Dihydro-6-phenyl-1H-1,4-diazepinium perchlorate (0.55 g, 2 mmoles) was dissolved in nitromethane (5 ml) and methyl fluorosulphonate ('magic methyl', 0.23 g, 2 mmoles) was added to it, and the mixture was kept at room temperature for 2 days. The addition of ether gave a solid which, after crystallisation with ethanolic perchloric acid had identical uv, m.p., and mixed m.p. to the starting material.

( ) Hydrolysis of 6-aryldiazepinium perchlorates

(i) Acid hydrolysis

Attempted hydrolysis of 2,3-dihydro-6-phenyl-1H-1,4-diazepinium perchlorate

6-Phenyldiazepinium perchlorate (0.27 g) was dissolved in conc. hydrochloric acid (8 ml) and water (2 ml). The mixture was heated under reflux for 6 hrs. The solvent was removed *in vacuo*, and the product was filtered off; it had an identical uv, m.p., and mixed m.p. to that of the starting material.

(ii) Alkaline hydrolysis

Formation of the sodium salt of phenylmalondialdehyde from 2,3-dihydro-6-phenyl-1H-1,4-diazepinium perchlorate

A solution of 6-phenyldiazepinium perchlorate (0.27 g) and sodium hydroxide (0.8 g) in methanol was heated under reflux for 4 hrs. Removal of the solvent *in vacuo* gave a solid which was filtered off. To this solid a methanolic solution of dianilinoethane and perchloric acid was added. A yellow crystalline product which formed after *ca* 1 hr at room temperature was filtered off. This product had the same m.p., mixed m.p., and uv as 1,4,6-triphenyldiazepinium perchlorate.

Formation of the sodium salt of α-naphthylmalondialdehyde from 2,3-dihydro-6-α-naphthyl-1H-1,4-diazepinium perchlorate

A methanolic solution of the α-naphthyldiazepinium perchlorate (0.3 g) and sodium hydroxide (0.8 g) was heated under reflux for 5 hrs. Removal of the solvent *in vacuo* gave a solid product which was identified by its reaction with a methanolic

solution of the dianilinoethane and perchloric acid. This reaction mixture gave a yellow solid which had the same m.p., mixed m.p. and uv as 1,4-diphenyl-6-α-naphthyldiazepinium perchlorate.

( ) Reactions of 6-halogeno-phenyldihydrodiazepinium salts with nucleophiles

(i) Thiourea

Thiourea (0.75 g, 1 mmole) in methanol (10 ml) was added to 6-p-bromophenyl-2,3-dihydro-1H-1,4-diazepinium perchlorate (0.3 g, 1 mmole) in methanol (10 ml), and the mixture was heated under reflux for ca 2 hrs. The mixture was then concentrated in vacuo, cooled, and addition of ether precipitated the starting material (0.25 g), identified by its unchanged uv spectrum, m.p. and mixed m.p. with the starting material.

(ii) Sodium Methoxide

Similarly, when the 6-p-bromophenyldiazepinium salt was heated under reflux with sodium methoxide [prepared by adding clean sodium (2 g) to methanol (20 ml)], it was recovered unchanged.

Likewise, 6-p-iodophenyl-2,3-dihydro-1H-1,4-diazepinium salt was unattacked by these nucleophiles.

( ) Reactions of 6-aryl substituted dihydrodiazepinium salts with amines

(i) 1,2-Diamines

2,3-Dihydro-1,4-dimethyl-6-phenyl-1H-1,4-diazepinium perchlorate

N,N'-Dimethylethylenediamine (0.88 g, 10 mmoles) was added to 6-phenyl-dihydrodiazepinium perchlorate (0.54 g, 2 mmoles) in methanol (200 ml) and the mixture was heated under reflux for 3 hrs. The solution was cooled and the crystalline product (0.56 g, 94%) was filtered off. It was identified as the 1,4-dimethyl-6-phenyldihydrodiazepinium perchlorate by its m.p., mixed m.p. with an authentic sample (62b) and by its λ_{max} values.

2,3-Dihydro-1,4-dimethyl-6-p-tolyl-1H-1,4-diazepinium perchlorate

A methanolic solution of the 6-p-tolyldiazepinium perchlorate (0.28 g, 1 mmole) and of N,N'-dimethylethylenediamine (0.88 g, 10 mmoles) was heated under reflux for 5 hrs, and the crystalline product (0.3 g, 98%) which resulted after working up the reaction mixture had the same m.p., mixed m.p., and λ_{max} values as an authentic sample (63b) of the 1,4-dimethyl-6-p-tolyldiazepinium perchlorate.

2,3-Dihydro-1,4-dimethyl-6-p-biphenyl-1H-1,4-diazepinium perchlorate

N,N'-Dimethylethylenediamine (0.88 g, 10 mmoles) was added to a solution of the 6-p-biphenyldiazepinium salt (0.34 g, 1 mmole) in acetonitrile (20 ml), and the mixture was heated under reflux for 6 hrs. Removal of the solvent in vacuo gave

crystals which were filtered off. The product (0.3 g, 82%) had m.p. 140° (from ethanolic perchloric acid), λ_{max} 370 nm (ε 10928), ν_{max} 1630, 1520, 1310, 1200, 1100, 910, 830, 770, 720 cm^{-1}, τ[($^2H_6$)DMSO] 1.98 (2H, s), 2.26-2.60 (9H, m), 6.16 (4H, s), 6.48 (6H, s). (Found: C, 60.48; H, 5.59; N, 7.41 $C_{19}H_{21}ClN_2O_4$ requires: C, 60.59; H, 5.61; N, 7.43%)

2,3-Dihydro-1,4-dimethyl-6-α-naphthyl-1H-1,4-diazepinium perchlorate (67b)

The product which was obtained when a methanolic solution of 6-α-naphthyldiazepinium perchlorate was heated under reflux for 6 hrs with N,N'-dimethylethylenediamine (tenfold) had the identical m.p., mixed m.p., and uv as an authentic sample (67b) of the 1,4-dimethyl-6-α-naphthyl derivative.

2,3-Dihydro-1,4-dimethyl-6-β-naphthyl-1H-1,4-diazepinium perchlorate (68b)

A mixture of the 6-β-naphthyldiazepinium perchlorate and N,N'-dimethylethylenediamine (ten fold) in methanol was heated under reflux for 6 hrs. The solvent was removed, and the crystalline product which was filtered off had the same m.p., mixed m.p., and uv as an authentic sample (68b) of the 1,4-dimethyl-6-β-naphthyl derivative.

When a solution of N,N'-dimethylethylenediamine (tenfold) was heated under reflux with the following dihydrodiazepinium perchlorates, only unchanged starting material was obtained in quantitative yield in each case:

2,3-Dihydro-6-*o*-tolyl-1H-1,4-diazepinium perchlorate; 2,3-Dihydro-5-methyl-6-phenyl-1H-1,4-diazepinium perchlorate; 2,3-Dihydro-6-*N*-pyridyl-1H-1,4-diazepinium diperchlorate.

Also, only starting material was obtained when an excess of ethylenediamine (10 times) solution was heated under reflux with a methanolic solution of 2,3-dihydro-1,4-dimethyl-6-phenyl-1H-1,4-diazepinium perchlorate.

(ii) Monoamines

Attempted transamination of 2,3-dihydro-6-phenyl-1H-1,4-diazepinium perchlorate with piperidine

A methanolic solution of the 6-phenyldiazepinium perchlorate (0.27 g) and piperidine (1.7g, 20 fold) was heated under reflux for 10 hrs. Removal of the solvent *in vacuo* gave a solid which was filtered off. It had m.p. 115-160° and the λ_{max} 252 and 322 nm showing that a different compound (mixture) had formed, but it could not be identified.

Reactions of 1,5-diaza-3-aryl-1,1,5,5-tetramethyl-1H-pentadienium perchlorates with piperidine

1,5-Diaza-1,1-dimethyl-5,5-pentamethylene-3-phenyl-1H-pentadienium perchlorate (72a)

Piperidine (0.51 g, 6 mmoles) in methanol (20 ml) was added to the pentadienium perchlorate (24) (0.9 g, 3 mmoles), in methanol (100 ml). The mixture was kept at room temperature for 2 hrs. Evaporation of the solvent in vacuo gave a crystalline product (0.5 g, 86%) which was filtered off and washed with ether. The product had m.p. 166-168° (from ethanol), λ_{max} 316 nm (ε 51763), ν_{max} 1570, 1280, 1200, 1080, 720 cm-1, τ [($^2H_6$)DMSO] 2.22 (2H, s), 2.55 (5H, m), 6.3-6.46 (2H, b), 6.67 (3H, s), 7.0-7.2 (2H, b), 7.48 (3H, s), 8.16-8.30 (4H, b), 8.6-8.8 (2H, b). (Found: C, 55.60; H, 6.80; N, 7.79 $C_{16}H_{23}ClN_2O_4$ requires: C, 56.05; H, 6.76; N, 8.17%).

1,5-Diaza-1,1,5,5-bispentamethylene-3-phenyl-1H-pentadienium perchlorate (73a)

A solution of the monopentamethylene pentadienium perchlorate (24) (0.68 g, 2mmoles) and piperidine (1.1 g, 12 mmoles) in methanol (50 ml) was heated under reflux for 2 hrs. The solvent was removed in vacuo, and a crystalline product (0.6 g, 70%) was filtered off and washed with ether. It had m.p. 228-230° (from acetonitrile), λ_{max} 316 nm (ε 53604), ν_{max} 1580, 1290, 1270, 1210, 1100, 1010, 720 cm^{-1}, τ [(TFA)], 2.4-2.6 (2H, b, m), 2.6-2.8 (5H, b, m), 6.6-6.8 (8H, b, m), 8.2-8.6 (12H, b, m). (Found: C, 58.68; H, 7.28; N, 7.32 $C_{19}H_{27}ClN_2O_4$ requires: C, 59.60; H, 7.10; N, 7.32%).

The bispentamethylene-3-phenyl compound was also obtained when the pentadienium salt (24) and piperidine (2 equivalents) were heated under reflux in the presence of acetonitrile for 10 hrs.

1,5-Diaza-1,1,5,5-bispentamethylene-3-p-tolyl-1H-pentadienium perchlorate (73b)

A mixture of the pentadienium perchlorate (61d) (3.1 g, 10 mmoles) and piperidine (8.5 g, 100 mmoles) in methanol (250 ml) was heated under reflux for 3 hrs. Removal of the solvent in vacuo gave the product (2.7 g, 69%) which was filtered off, and had m.p. 174-176° (from acetonitrile), λ_{max} 316 nm (ε 46439), ν_{max} 1570, 1280, 1070, 720 cm^{-1}, τ [($^2H_6$)DMSO], 2.32 (2H, s), 2.72-2.76 (4H, d), 6.36-6.60 (4H, b), 7.0-7.30 (4H, b), 7.66 (3H, s), 8.2-8.6 (8H, b), 8.6-8.86 (4H, b). (Found: C, 59.83; H, 7.16; N, 7.1 $C_{20}H_{29}ClN_2O_4$ requires: C, 60.52; H, 7.36; N, 7.08%).

1,5-Diaza-1,1-dimethyl-5,5-pentamethylene-3-o-tolyl-1H-pentadienium perchlorate (72c)

A mixture of the pentadienium perchlorate (61f) (0.94 g, 3 mmoles) and piperidine (0.51 g, 6 mmoles) in methanol (150 ml) was kept at room temperature for 22 hrs. Removal of the solvent in vacuo gave a crystalline product (0.85 g, 80%) which was filtered off and washed with ether; it had m.p. 146-150° (from ethanol), λ_{max} 316 nm (ε 39491), ν_{max} 1570, 1285, 1200, 1100, 750, 720 cm^{-1}, τ [($^2H_6$)Acetone], 2.37 (2H, s), 2.64-2.72 (4H, m), 6.26-6.40 (2H, b, t), 6.66 (3H, s), 6.98-7.18 (2H b, t), 7.47 (3H s), 7.72 (3H, s), 8.2-8.40 (4H, b), 8.6-8.8 (2H, b). (Found: C, 56.07; H, 6.88; N, 7.72 $C_{17}H_{25}ClN_2O_4$ requires: C, 57.19; H, 7.06; N, 7.85%).

1,5-Diaza-1,1,5,5-bispentamethylene-3-α-naphthyl-1H-pentadienium perchlorate (73c)

Piperidine (0.85 g, 10 mmoles) was added to the pentadienium perchlorate (61h) (1.7 g, 5 mmoles) in acetonitrile (150 ml) and the mixture was heated under reflux for 10 hrs. Removal of the solvent in vacuo gave crystals which were filtered off and washed with ether. The product (1.2 g, 81%) had m.p. 210° (from acetonitrile), λ_{max} 317 nm (ε47393), ν_{max} 1570, 1290, 1260, 1200, 1100, 1010, 790, 720 cm^{-1}, τ [($^2H_6$)DMSO], 1.92-1.98 (2H, m), 2.0-2.47 (7H, m), 6.38-6.54 (4H, b, t), 7.4-7.52 (4H, b), 8.26-8.72 (8H, b, d), 8.92-9.3 (4H, b). (Found: C, 62.88; H, 6.75; N, 6.62 $C_{23}H_{29}ClN_2O_4$ requires: C, 63.79; H, 6.75; N, 6.47%).

1,5-Diaza-1,1,5,5-bispentamethylene-3-β-naphthyl-1H-pentadienium perchlorate (73d)

A solution of the pentadienium perchlorate (61i) (1.7 g, 5 mmoles) and piperidine (0.85 g, 10 mmoles) in acetonitrile (150 ml) was heated under reflux for 10 hrs. The solvent was removed in vacuo and a crystalline product (1 g, 79%) was filtered off and washed with ether; it had m.p. 198-200° (from acetonitrile), λ_{max} 318 nm (ε40272), ν_{max} 1570, 1270, 1210, 1100, 780, 760, 720 cm^{-1}, τ [($^2H_6$)DMSO] 1.93-2.0 (2H, m), 2.09-2.58 (7H, m), 6.36-6.5 (4H, b), 7.12-7.36 (4H, b), 8.17-8.66 (8H, b, d), 8.68-9.0 (4H, b). (Found: C, 62.97; H, 6.78; N, 6.26 $C_{23}H_{29}ClN_2O_4$ requires: C, 63.79; H, 6.75; N, 6.47%).

Although the percentage of hydrogen and nitrogen elemental analyses in these compounds was found to be reasonably acceptable, the carbon percentage was low in each case.

Part II

Preparation of 1,5-Benzodiazepinium Salts

1,5-Benzodiazepines were prepared as described by Thiele and Steimmig[150]. The typical method is given below:

2,4-Dimethyl-3H-1,5-benzodiazepinium perchlorate (108)

O-Phenylenediamine (1.08 g, freshly purified by vacuum sublimation) dissolved in ethanol (10 ml) was added to acetylacetone in glacial acetic acid (1 ml). The mixture was heated under reflux for 10 mins, cooled and perchloric acid (5 ml, 60%) was added, and was kept at 0° overnight. The dark purple crystals were filtered off and washed with little cold ethanol and then with ether; it had m.p. 215-216°.

Similarly the 2,4-diphenyl-3H-1,5-benzodiazepinium perchlorate (115), 2,4,7-trimethyl-3H-1,5-benzodiazepinium perchlorate (112), and 7-methyl-2,4-diphenyl-3H-1,5-benzodiazepinium perchlorate (116) were prepared.

(For ^{1}H n.m.r. spectra of these compounds see Table 4).

The 1,5-benzodiazepine bases were prepared using the experimental procedure described by I.L. Finar[199]. A typical method is given below.

2,4-Diphenyl-3H-1,5-benzodiazepine base

Dibenzoylmethane (11.2 g, 50 mmoles) dissolved in ethanol (50 ml) and glacial acetic acid (18 ml) was added to freshly prepared purified o-phenylenediamine (5.4 g, 50 mmoles). The mixture was heated under reflux for 3 hrs, cooled, and the colourless product was filtered off and washed with ether; it had m.p. 148° (from ethanol), lit.[199] m.p. 140-141°.

Reactions with Electrophiles

Bromination of 1,5-benzodiazepinium salts

The bromination of 1,5-benzodiazepinium perchlorates were carried out in an excess of glacial acetic acid under the conditions used by R. Williams and co-workers[179]. A typical method is given below.

2,4-Bis(dibromomethyl)-1,5-benzodiazepinium bromide

Bromine (4.8 g, 30 mmoles) was added dropwise to a stirred solution of the corresponding unsubstituted 1,5-benzodiazepinium perchlorate (108) (1.36 g, 5 mmoles) in glacial acetic acid (900 ml). The mixture was stirred for a further 3 hrs, and kept at room temperature overnight. The solvent was concentrated *in vacuo*, cooled, and ether added. The product (70%) was filtered off; it had m.p. $> 350^{\circ}$. (Found: (C, 23.33; H, 1.56; N, 5.09 $C_{11}H_9N_2Br_5$ requires: C, 23.23; H, 1.59; N, 4.92%)

Similarly, the 2,4-dimethyl-1,5-benzodiazepinium perchlorate (108) with 4-fold bromine gave 2-dibromomethyl-4-bromomethyl-1,5-benzodiazepinium bromide (110), and when eight equivalents of bromine was treated with 2,4,7-trimethylbenzodiazepinium salt only 2,4-bis(dibromomethyl)-7-methyl-1,5-benzodiazepinium bromide (113) was isolated.

(For ^1H n.m.r. spectra of these compound see Table 4.)

Part III

Preparation of Bisoxoenamines

The bisoxoenamines were prepared by the following method:

Bisoxoenamine (125a)

Ethylenediamine (0.3 g, 5 mmoles) in methanol (5 ml) was added to acetylacetone (1 g, 10 mmoles) and the mixture was kept at room temperature overnight. A crystalline product was filtered off; it had m.p. 115-116° (from ethanol), lit. m.p.[166] 111°,

Bisoxoenamine (125b)

A methanolic solution of ethylenediamine (0.6 g, 10 mmoles) was added to benzoylacetone (3.2 g, 20 mmoles) dissolved in warm methanol (15 ml). The mixture was kept at room temperature overnight. The product (6.3 g, 90%) was filtered off; it had m.p. 183-185° (from ethanol), λ_{max} 341 and 258 nm (rough), ν_{max} 3180, 3060, 1610, 1270, 1210, 1090, 1020, 970, 930, 850, 820, 740 cm^{-1}, τ [($^2H_6$)DMSO], 2.52-2.66 (10H, m), 4.22 (2H, s), 6.62 (4H, s), 8.1 (6H, s). (Found: C, 64.30; H, 9.0; N, 12.49 $C_{12}H_{20}N_2O_2$ requires: C, 64.28; H, 8.97; N, 12.5%)

Bisoxoenamine (125c)

Benzoylacetone (1.6 g, 10 mmoles) was added to a methanolic solution of 1,3-diaminopropane (0.35 g, 5 mmoles). The mixture was kept in the refrigerator for 3 days. A colourless crystalline product (3.2 g, 92%) was filtered off; it had m.p. 86-88° (from ethanol), λ_{max} 345 and 248 nm (ε 30316 and 15158), ν_{max} 3220, 1620, 1270, 1210, 1090, 970, 850, 820, 735 cm^{-1}, τ [($^2H_6$)Acetone] 2.54-2.68 (10H, m), 4.23 (2H, s), 6.4-6.62 (6H, m), 7.93 (6H, s).

(Found: C, 76.04; H, 7.33; N, 7,68 $C_{23}H_{26}N_2O_2$ requires: C, 76.14; H, 7.17; N, 7.72%)

Bisoxoenamine (125d)

1,3-Diaminopropane (0.35 g, 5 mmoles) was added to a cooled solution of acetylacetone (1 g, 10 mmoles) in methanol (5 ml). The mixture was stirred at room temperature for 1 hr, and then kept in the refrigerator overnight. The product (2.4 g, 90%) was filtered off; it had m.p. 36-40°, λ_{max} 294 mμ (rough), ν_{max} 3180, 1610, 1260, 1090, 970, 850 cm^{-1}, τ [($^2H_6$)Acetone], -(0.56)-(-0.74, NH, br), 5.04 (2H, s), 6.42-6.6 (6H, m), 8.11-8.14 (12H, d). (Found: C, 65.60; H, 9.30; N, 11.77 $C_{13}H_{22}N_2O_2$ requires: C, 65.54; H, 9.24; N, 11.76%)

Bisoxoenamine (125e)

1,2-Diaminocyclohexane (0.55 g, 5 mmoles) was added to a methanolic solution of acetylacetone (1 g, 10 mmoles). The mixture was kept at room temperature for 2 days. The product (1.4 g, 60%) was filtered off; it had m.p. 138-139° (from ethanol), lit. m.p. 136.5°.

Methylation of Bisoxoenamine Products Using Methyl Fluorosulphonate to give Bisazaoxapentadienium Salt

Methylation of compound (125a) to give bisazaoxapentadienium salt (126a).

The bisoxoenamine (125a, 1.1 g, 5 mmoles) was dissolved in dry methylene chloride (10 ml), and methylfluorosulphonate (1.1 g, 10 mmoles) was added. The mixture was kept at room temperature for 1 hr and ether was added to complete crystallisation of the

product (2.2 g, 97%), which was filtered off, and finally washed with ether. It had m.p. 143-144° (from acetonitrile), λ_{max} 290 nm (rough), ν_{max} 3260, 1590, 1270, 1070, 930, 800, 720 cm^{-1} τ[($^2H_6$)DMSO] 5.04 (2H, s), 6.52 (6H, s), 6.57-6.63 (4H, m), 8.12-8.16 (12H, d). (Found: C, 36.70; H, 5.99; N, 6.12 $C_{14}H_{26}F_2N_2O_8S_2$ requires: C, 36.94; H, 5.75; N, 6.18%)

Compounds (125b-e) were reacted similarly with methyl-fluorosulphonate. The methylated products of bisoxoenamine compounds (126b-e), however, were not isolated but reacted further with the appropriate diamines.

Cyclisation of the methylated products with diamines

5,7,12,14-Tetramethyl-1,4,8,11-tetra-azatetradecadienedi-ium salt (127a)

Ethylenediamine (0.3 g, 5 mmoles) was added to a solution of bisazaoxopentadienium salt (126a) (2.2 g, 5 mmoles) in methanol (200 ml). The mixture was heated under reflux for 0.5 hr, and the solvent was removed in vacuo. The product (2 g, 90%) was filtered off; it had m.p. 245-246° (from acetonitrile), λ_{max} 295 nm (rough), ν_{max} 3200, 1270, 1230, 1090, 970, 820 cm^{-1}, τ[($^2H_6$)DMSO], 0.7-0.84 (NH, br), 4.15 (2H, br), 5.9-6.34 (4H, br), 7.64 (12H, s). (Found: C, 37.53; H, 6.06; N, 12.67 $C_{14}H_{26}F_2N_4O_6S_2$ requires: C, 37.46; H, 5.80; N, 12.93%)

5,14-Dimethyl-7,12-diphenyl-1,4,8,11-tetra-azatetradecadiene-di-ium salt (127b)

The methylated intermediate product (126b) (0.92 g, 2 mmoles) was dissolved in methanol (100 ml) and ethylenediamine (0.12 g, 2 mmoles) was added to the solution. The mixture was heated

under reflux for 3 hrs. Removal of the solvent in vacuo gave a crystalline product (0.9 g, 82%), which was filtered off and washed with ether; it had m.p. 128-130° (from acetonitrile), λ_{max} 341 and 258 nm (ε 36480 and 2333), ν_{max} 3300, 1620, 1530, 1270, 1090, 970, 850 cm^{-1}, τ [($^2H_6$)DMSO], 2.53 (10H, s), 4.94 (2H, s), 5.7-5.96 (8H, br), 7.93 (6H, s). (Found: C, 50.36; H, 5.30; N, 9.85 $C_{24}H_{30}F_2N_4O_6S_2$ requires: C, 50.29; H, 5.28; N, 9.78%)

Attempted preparation of 6,16-dimethyl-8,14-diphenyl-1,5,9,13-tetra-azahexadecadiendi-ium salt

1,3-Diaminopropane (0.7 ml, 10 mmoles) was added to a methanolic solution of the methylated intermediate (126c) generated in situ by reaction of the compound (125c) with methyl fluorosulphonate. The mixture was heated under reflux for 3 hrs. Removal of the solvent gave a jelly-like material which showed λ_{max} ca 325 nm in its u.v. spectrum. The product, could not, however, be obtained in a solid form.

Similarly, an attempted cyclisation of the methylated intermediate compounds (126d and 126c) prepared in situ from (125d and 125e) with 1,3-diaminopropane and with ethylenediamine respectively were unsuccessful, although the shifts to longer wavelengths in the u.v. spectra of these reaction mixtures indicated that the cyclised products may have been formed.

Preparation of a 16-membered ring compound

Ammonia was passed through a refluxing solution of the p-nitrophenyl pentadienium perchlorate (61e, 1.7 g, 5 mmoles) in methanol (250 ml) for 15 mins. 1,3-Diaminopropane (0.4 g,

5 mmoles) was added to the cool ed mixture which was then heated under reflux for 5 hrs. The mixture was kept at room temperature overnight. Black needles, (ca 10%), were filtered off; it had m.p. 252°, λ_{max} 446 and 310 nm (rough, in acetonitrile). (Found: C, 61.98; H, 5.92; N, 18.29 $C_{24}H_{26}N_6O_4$ requires: C, 62.0; H, 6.0; N, 18.1%). The product was insoluble in a variety of standard solvents, and its ^1H n.m.r was not recorded. The compound (128a) was identified by its accurat e mass number, and elemental analysis.

The filtrate from the remainder of the reaction mixture was concentrated by removal of the solvent in vacuo, cooled, and ether was added to it. The product was filtered off; it had λ_{max} 460 and 303 nm (solution spectrum) but it could not be identified.

Similar attempts to isolate the 16-membered ring compounds made from p-tolyl, p-chlorophenyl, and p-bromophenyl pentadienium perchlorates were unsuccessful.

Reactions with Electrophile

Attempted bromination of the 14-membered ring compound (127a)

The 14-membered ring compound (127a) (0.4 g, 1 mmole) was dissolved in methanol (50 ml). Bromine (0.16 g, 1 mmole) in methanol (20 ml) was added slowly over a period of 0.5 hr. The mixture was stirred for 6 hrs, kept at room temperature overnight. The solvent was removed, and the crystalline product was filtered off; it had an identical u.v. spectrum, and the same m.p. and mixed m.p. to the starting material.

Part IV

Preparations of 1,2-dihydro-1,3-dimethyl-2-oxo- and 2-thioxo-5-arylpyrimidinium perchlorates using Arylmalondialdehyde Salts

1,2-Dihydro-1,3-dimethyl-2-oxo-5-phenylpyrimidinium perchlorate (134a)

N,N'-Dimethylurea (1.76 g, 20 mmoles) was added to phenylmalondialdehyde liberated *in situ* by addition of perchloric acid (60%, 4 g, 40 mmoles) to a solution of the sodium salt of phenylmalondialdehyde (3.4 g, 20 mmoles) in methanol (60 ml). A crystalline product (3.6 g, 60%) was filtered off and washed with water and then with ether; it had m.p. 278-280°, λ_{max} 252 and 360 nm (ε 16800 and 2750), ν_{max} 1810, 1570, 1310, 1080, 960, and 720 cm^{-1}, τ [($^2H_6$)DMSO], 0.41 (2H, s), 2.2-2.5 (5H, c), 6.14 (6H, s). (Found: C, 47.5; H, 4.5; N, 9.2 $C_{12}H_{13}ClN_2O_5$ requires: C, 47.95; H, 4.35; N, 9.3%)

1,2-Dihydro-5-p-methoxyphenyl-1,3-dimethyl-2-oxopyrimidinium perchlorate (134c)

Prepared like its phenyl analogue, crystals of this perchlorate were filtered off after 10 mins (70%) and washed with water, and had m.p. 232° (from propan-2-ol-dimethylformamide) λ_{max} 272 and 390 nm (ε 1300 and 17200), ν_{max} 1715, 1580, 1290, 1180, 1100, 835, and 760 cm^{-1}, τ [($^2H_6$)DMSO] 0.54 (2H, s) 2.60 (4H, AA'BB' system), 6.13 (3H, s), 6.17 (6H, s). (Found: C, 47.45; H, 4.55; N, 8.65 $C_{13}H_{15}ClN_2O_5$ requires: C, 47.15; H, 4.55; N, 8.45%)

1,2-Dihydro-1,3-dimethyl-5-p-nitrophenyl-2-oxopyrimidinium perchlorate (134e)

N,N'-Dimethylurea (1.76 g, 20 mmoles) was added to p-nitrophenylmalondialdehyde liberated in situ by addition of perchloric acid (60%, 4 ml, 40 mmoles) to a solution of the sodium salt of p-nitrophenylmalondialdehyde (4.2 g, 20 mmoles) in methanol (60 ml). The colourless crystals which had formed after ca 1 hr at room temperature were filtered off and finally washed with water. The product (4.4 g, 65%) had m.p. 252° (from acetonitrile), λ_{max} 242 and 353 nm (ε 85583 and 3456), ν_{max} 2000, 1740, 1640, 1580, 1515, 1310, 1100, 970, 850, 765 cm^{-1}, τ[($^2H_6$)DMSO], 0.4-0.7 (2H, br), 1.52-1.63 (2H, d), 1.97-2.06 (2H, d), 6.21 (6H, s) (Found: C, 42.0; H, 3.53; N, 12.33 $C_{12}H_{12}ClN_3O_7$ requires: C, 41.8; H, 3.48; N, 12.15%)

5-p-Bromophenyl-1,2-dihydro-1,3-dimethyl-2-oxopyrimidinium perchlorate (134f)

This salt (5.4 g, 71%) prepared from N,N'-dimethylurea (1.76 g, 20 mmoles), perchloric acid (60%, 4 ml, 40 mmoles) and a solution of the sodium salt of p-bromophenylmalondialdehyde (5g, 20 mmoles) in methanol (60 ml) had m.p. 230-232° (from acetonitrile), λ_{max} 360 (br) and 275 (br) nm, ν_{max} 1720, 1580, 1300, 1100, 960, 870, 750 cm^{-1}, τ[($^2H_6$)DMSO] 0.42 (2H, s), 2.14-2.23 (2H, d), 2.28-2.36 (2H, d), 6.2 (6H, s). (Found: C, 37.81; H, 3.08; N, 7.36 $C_{12}H_{12}BrClN_2O_5$ requires: C, 37.97; H, 3.18; N, 7.36%)

1,2-Dihydro-1,3-dimethyl-5-o — tolyl-2-oxopyrimidinium perchlorate (135)

N,N'-Dimethylurea (1.76 g, 20 mmoles) was added to o-tolylmalondialdehyde liberated in situ by addition of perchloric acid (60%, 4 ml, 40 mmoles) to a solution of the sodium salt of o-tolylmalondialdehyde (3.6 g, 20 mmoles) in methanol (60 ml). A crystalline product (4 g, 64 %) which had formed after 3 hrs was filtered off and washed with water and finally with ether; it had m.p. 230° (from acetonitrile), λ_{max} 346 (br) and 250 (br) nm, ν_{max} 1720, 1560, 1310, 1100, 960, 760 cm^{-1}, τ [($^2H_6$)DMSO], 0.74 (2H, s), 2.56-2.64 (4H, m), 6.23 (6H, s), 7.64 (3H, s) (Found: C, 52.43; H, 5.04; N, 9.04 $C_{13}H_{15}ClN_2O_4$ requires: C, 52.27; H, 5.06; N, 9.38%)

1,2-Dihydro-1,3-dimethyl-5-phenyl-2-thioxopyrimidinium perchlorate (134b)

Methanol (5 ml), perchloric acid (60%, 0.6 g, 6 mmoles), and N,N'-dimethylthiourea (0.2 g, 2 mmoles) were added successively to the sodium salt of phenylmalondialdehyde (0.34 g, 2 mmoles), and the mixture was kept overnight at room temperature. The product (0.2 g, 32%) was filtered off and washed with water, and had m.p. 284-288° (from ethanol), λ_{max} 222 (shoulder) and 307 nm (ε 19300), ν_{max} 1590, 1300, 1100, 940, 860, 760 cm^{-1}, τ [($^2H_6$)DMSO], 0.23 (2H, s), 2.53 (5H, m), 6.53 (6H, s). (Found: C, 45.75; H, 4.65; N, 8.65 $C_{12}H_{13}ClN_2O_4S$ requires: C, 45.35; H, 4.1; N, 8.85%)

1,2-Dihydro-5-p-methoxyphenyl-1,3-dimethyl-2-thioxopyrimidinium perchlorate (134d)

Prepared as the 5-phenyl analogue this salt (34%) had m.p. 145-146° (from ethanol), λ_{max} 232 and 317 nm (ε 12500 and 14400), ν_{max} 1580, 1300, 1180, 1100, 1060, 930, 835, and 720 cm^{-1}, τ[($^2H_6$)DMSO], 0.33 (2H, s), 2.56 (4H, AA'BB' system), 6.15 (3H, s), 6.16 (6H, s). (Found: C, 44.2; H, 5.0; N, 7.6 $C_{13}H_{15}ClN_2O_5S$ requires C, 44.95; H, 4.35; N, 8.05%)

Reactions with Electrophiles

Attempted bromination of 1,2-dihydro-1,3-dimethyl-2-oxo-5-phenylpyrimidinium perchlorate (134a)

Bromine (0.64 g, 4 mmoles) was added dropwise to a stirred solution of the corresponding unsubstituted phenylpyrimidinium perchlorate (134a) (1.2 g, 4mmoles) in warm methanol (100 ml) at 35°. The mixture was stirred for 4 hrs, solvent was removed in vacuo, cooled, and ether added. The product (1.1 g) was filtered off; it had the same m.p. and mixed m.p. and the λ_{max} values as the starting material (134a).

The same result was obtained when pyridine was used as a solvent.

Reaction with N-Bromosuccinimide

The starting material was obtained in quantitative yield when the above experiment was repeated with N-bromosuccinimide in glacial acetic acid.

Reactions with Piperidine

The 5-arylpyrimidinium salts(134a-f) and (135) were severally dissolved in deuteriated dimethyl sulphoxide (0.5 ml) in the n.m.r. tubes and piperidine (50 mg) was added in each case. The reaction was followed by the ^{1}H n.m.r. spectrum in each case, and the following results were obtained.

Proton N.m.r. Spectra of Adducts of Compounds (134a-f) and (135)

Compound	(H-4)	(H-6)	(H-1,-3)	Others
134a	4.96	3.13	6.83,7.01	2.4-2.7 (Ph)
134c	4.98	3.28	6.94,7.01	2.54-2.63 (Ph) 3.1-3.2 (Ph); 6.26 (OMe)
134e	4.98	3.26	6.91,7.01	1.55-1.66 (Ph) 1.98-2.1 (Ph)
134f	4.94	3.22	6.92,7.01	2.18-2.2 (Ph) 2.29-2.34 (Ph)
135	4.96	3.20	6.87,7.01	2.59-2.67(Ph); 7.67 (Me)
134b	4.74	2.86	6.5,6.6	2.4-2.78 (Ph)
134d	4.78	3.16	6.52,6.6	2.47-2.58 (Ph) 2.98-3.06 (Ph); 6.24 (OMe)

Appendix

Publications

1. D. Lloyd, R.K. Mackie, H. McNab, D.R. Marshall and K.S. Tucker, Tetrahedron, 32 (1976)

2. D. Lloyd, H. McNab and K.S. Tucker, J.Chem.Soc.Perkin Trans. I, 1862 (1977)

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